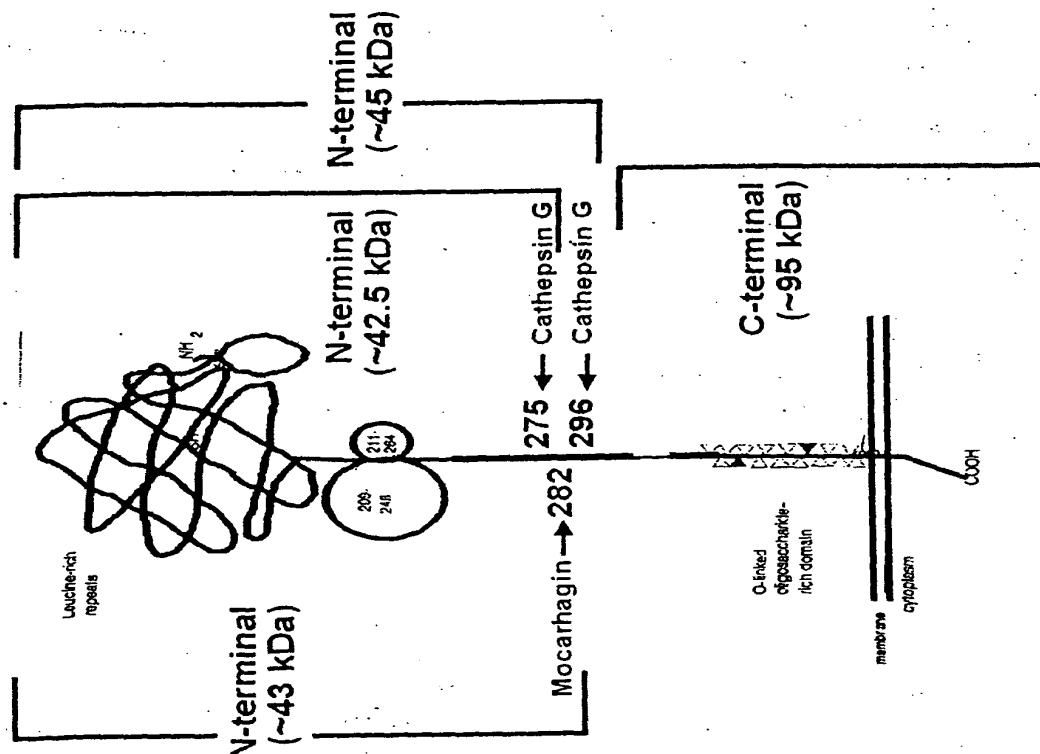


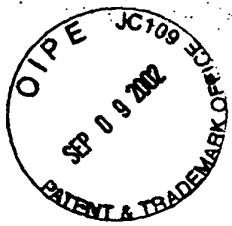
Cleavage sites of endoproteases on the α -chain of GPIb



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FIG. 1

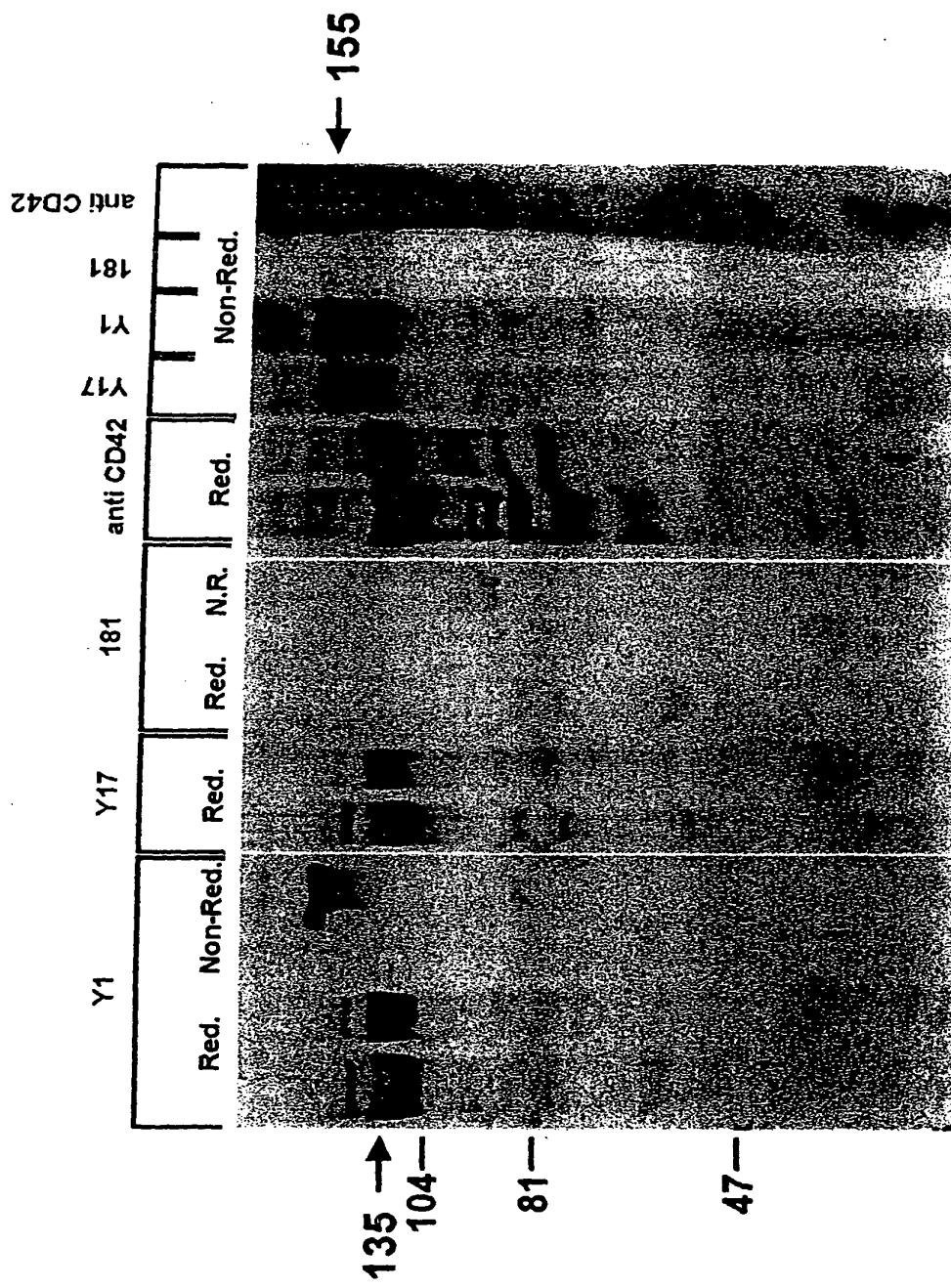




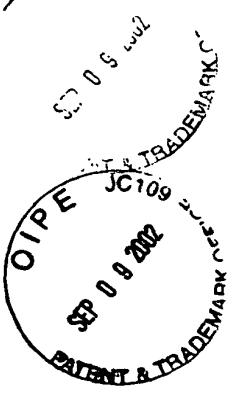
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FIG. 2

Binding of Y1 and Y17 to platelets in reduced and non-reduced conditions



**Characterization of Optimal Determinants
for Binding of Y1 to It's Ligands**



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FIG. 3

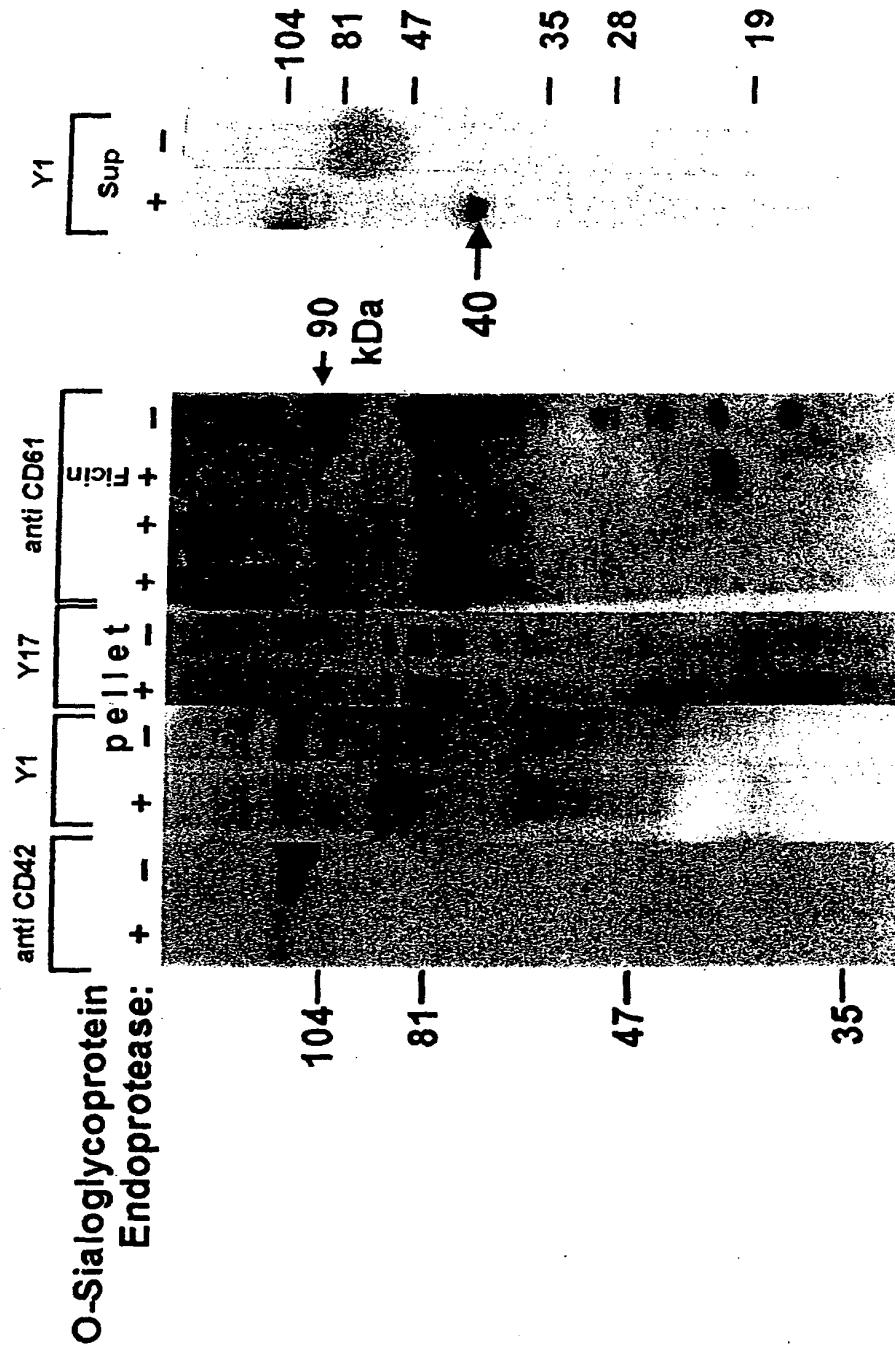
	Platelets/GC	KG1/RP-HPLC #4
Rec: GP1b 1-340	-	
GP1b 1-480	-	
Glycanase: N	+	+++
N+O	+	+++
Proteases: Mocarhagin	++ (~40kD)	-
O-Sialo Peptidase	++ (~40kD)	-
Ficin	-	-
Trypsine	++ (~40kD)	-
Elastase	++ (~40kD)	++
Sulfatase (Aryl)		-/+



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FIG. 4

**Cleavage of platelets GPIb by O-Sialoglycoprotein
abolishes binding of both Y1 and Y17**

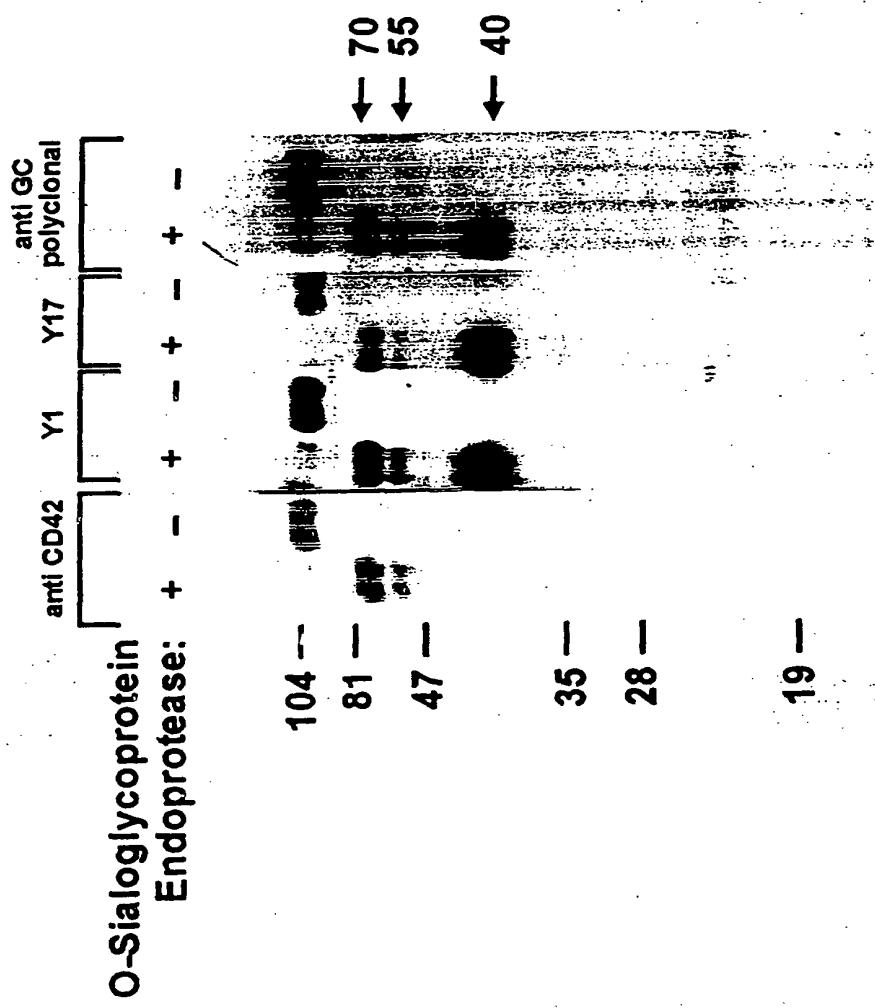


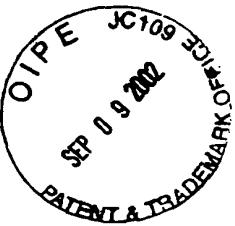


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FIG. 5

Y1 and Y17 binds similar gly cocalycin fragments after cleavage by O-Sialoglycoprotein Endoprotease

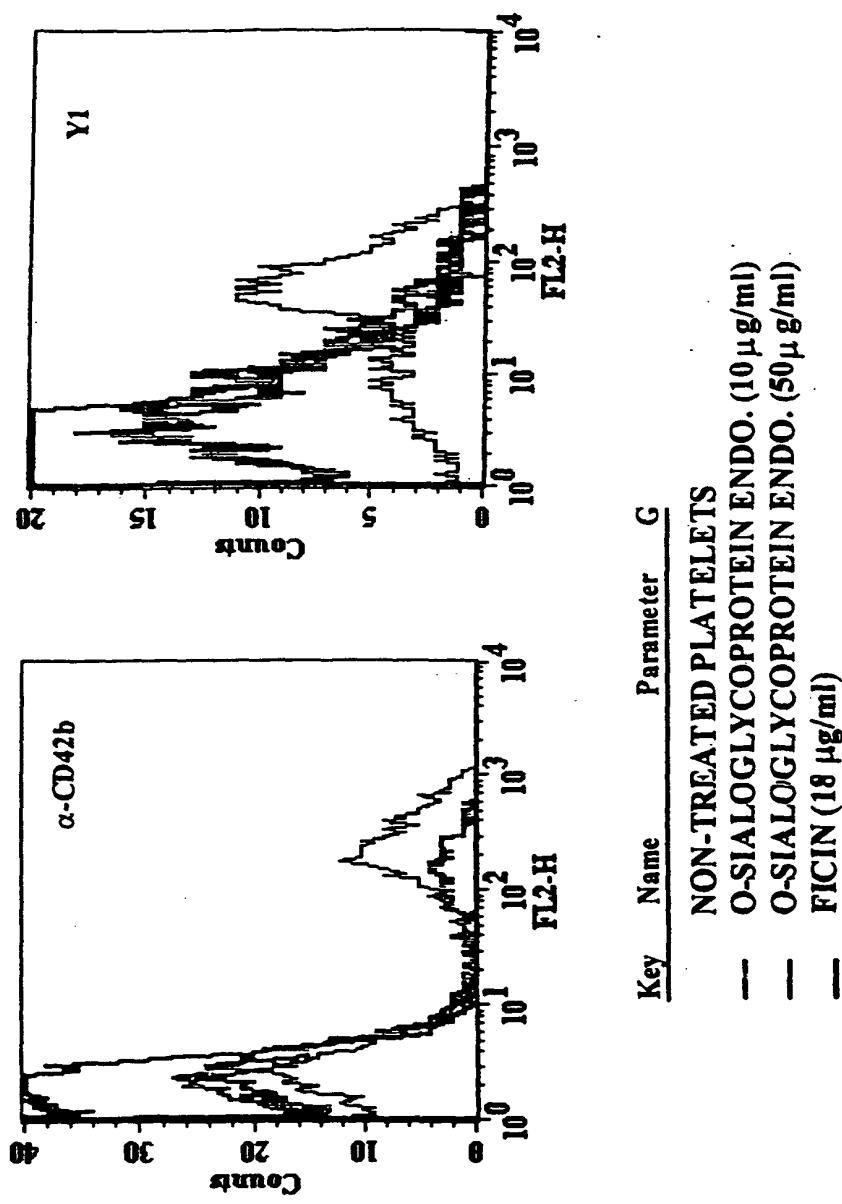




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Specific GPIIb Proteolysis Abolishes Y1 Binding to Platelets

FIG. 6

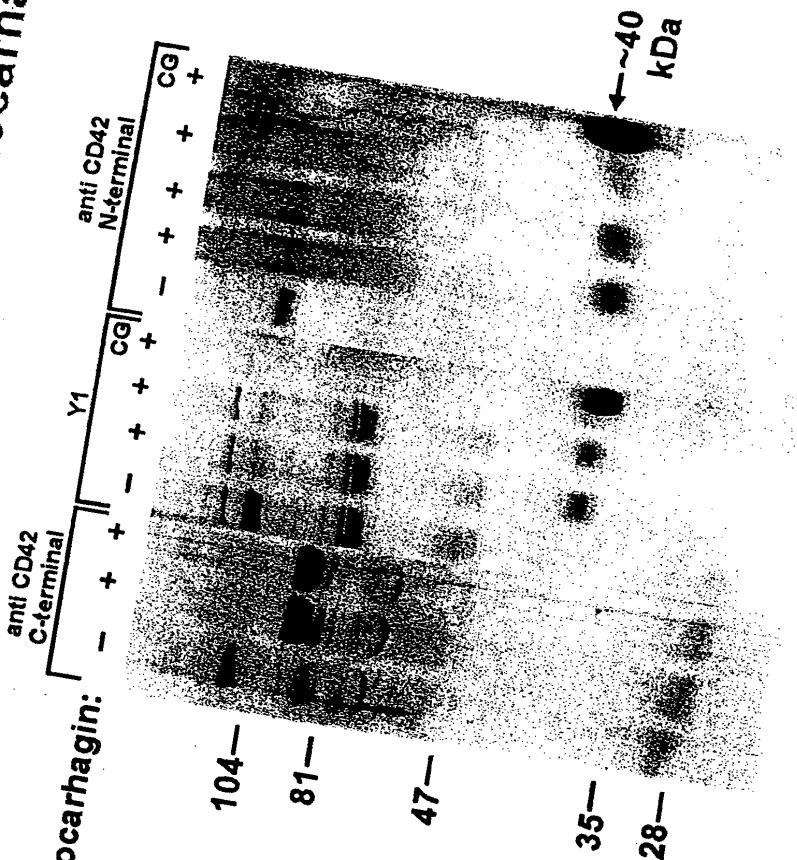


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**Y1 binds N-terminal (His-1 - Glu 282) fragment of
platelet GPIb after cleavage by mocardagin**

FIG. 7

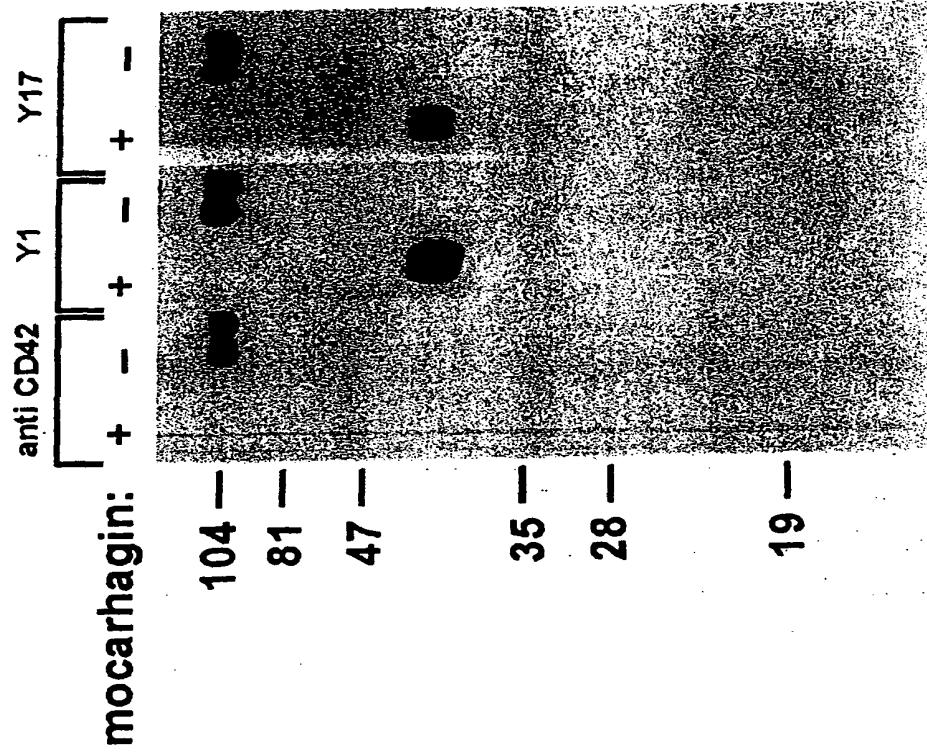




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FIG. 8

**Binding of Y1 and Y17 to glycocalyxin after
cleavage by molarhagin**

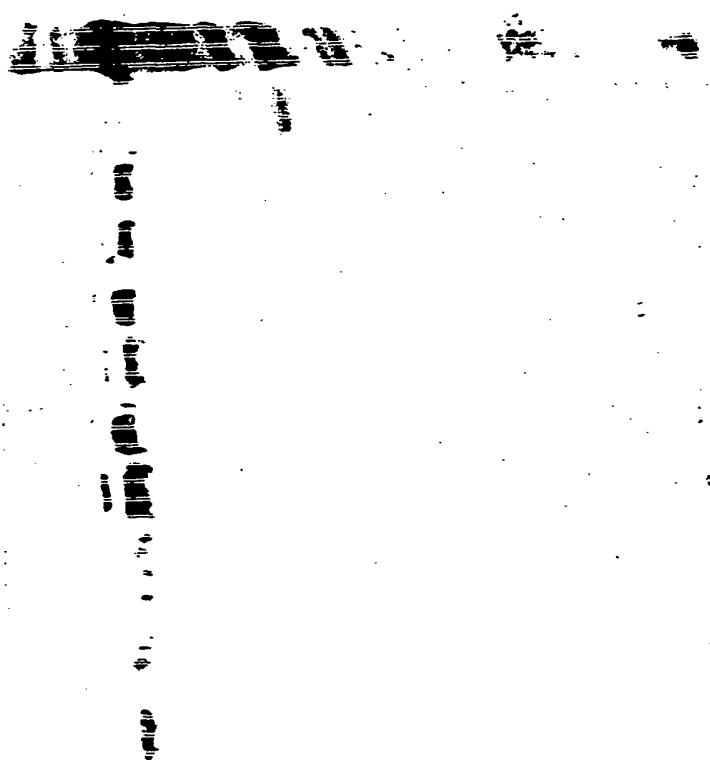
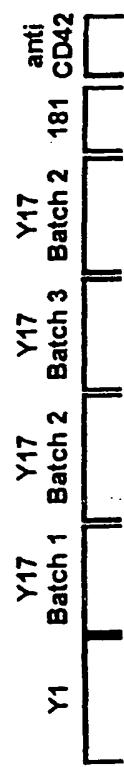




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FIG. 9

Binding of Y1 and Y17 to platelets



104—

81—

47—

35—

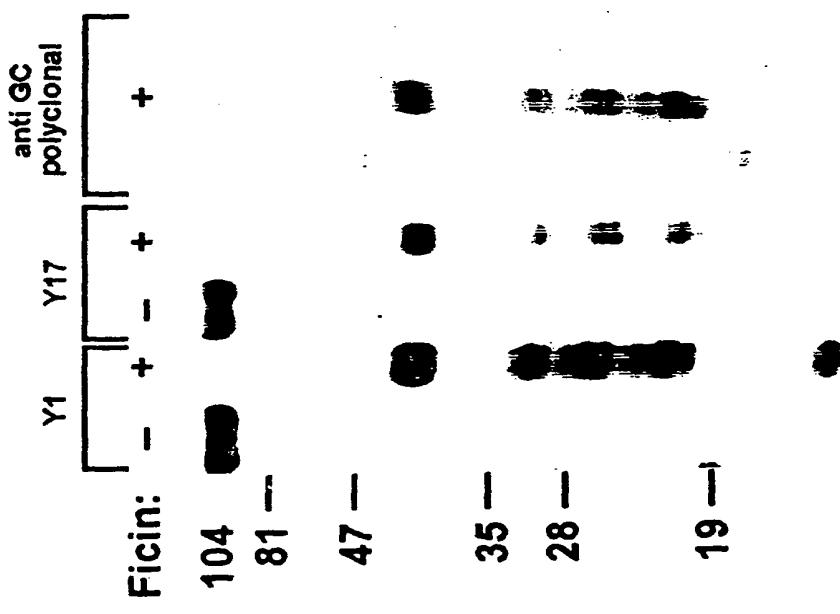
28—



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FIG. 10

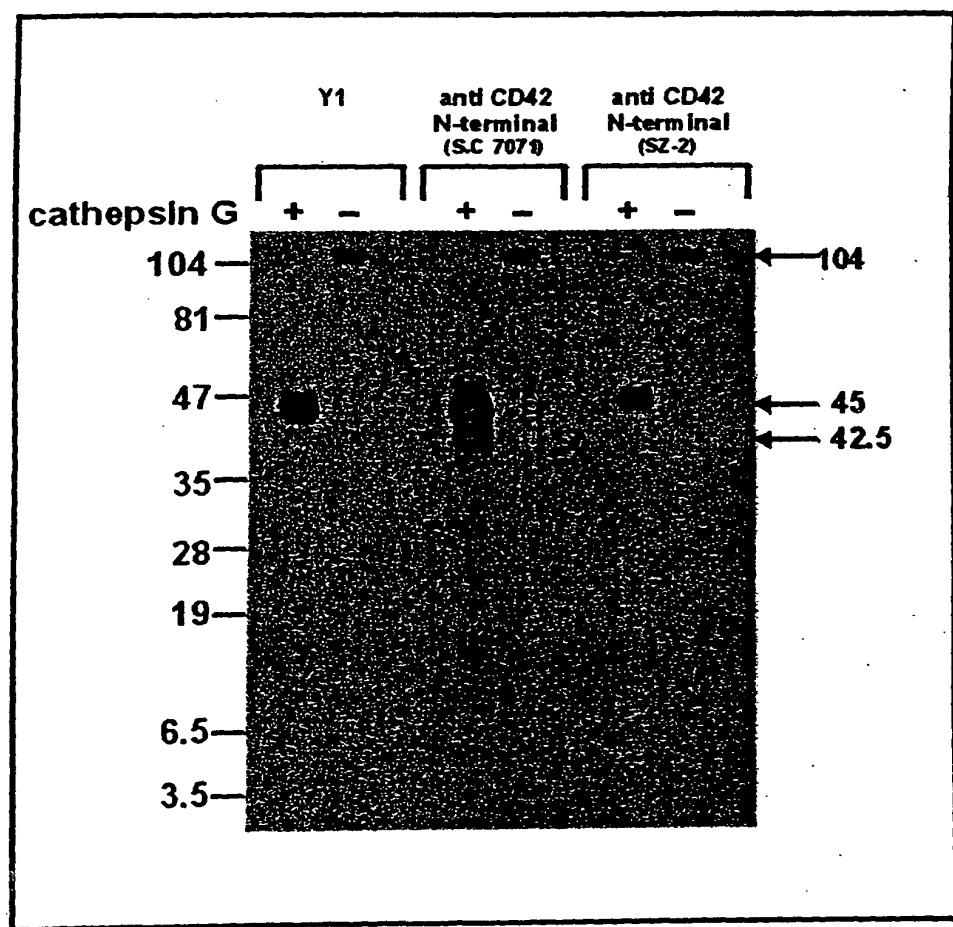
γ_1 and γ_{17} bind glycocalyxin similar after cleavage by Ficin





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FIG. 11

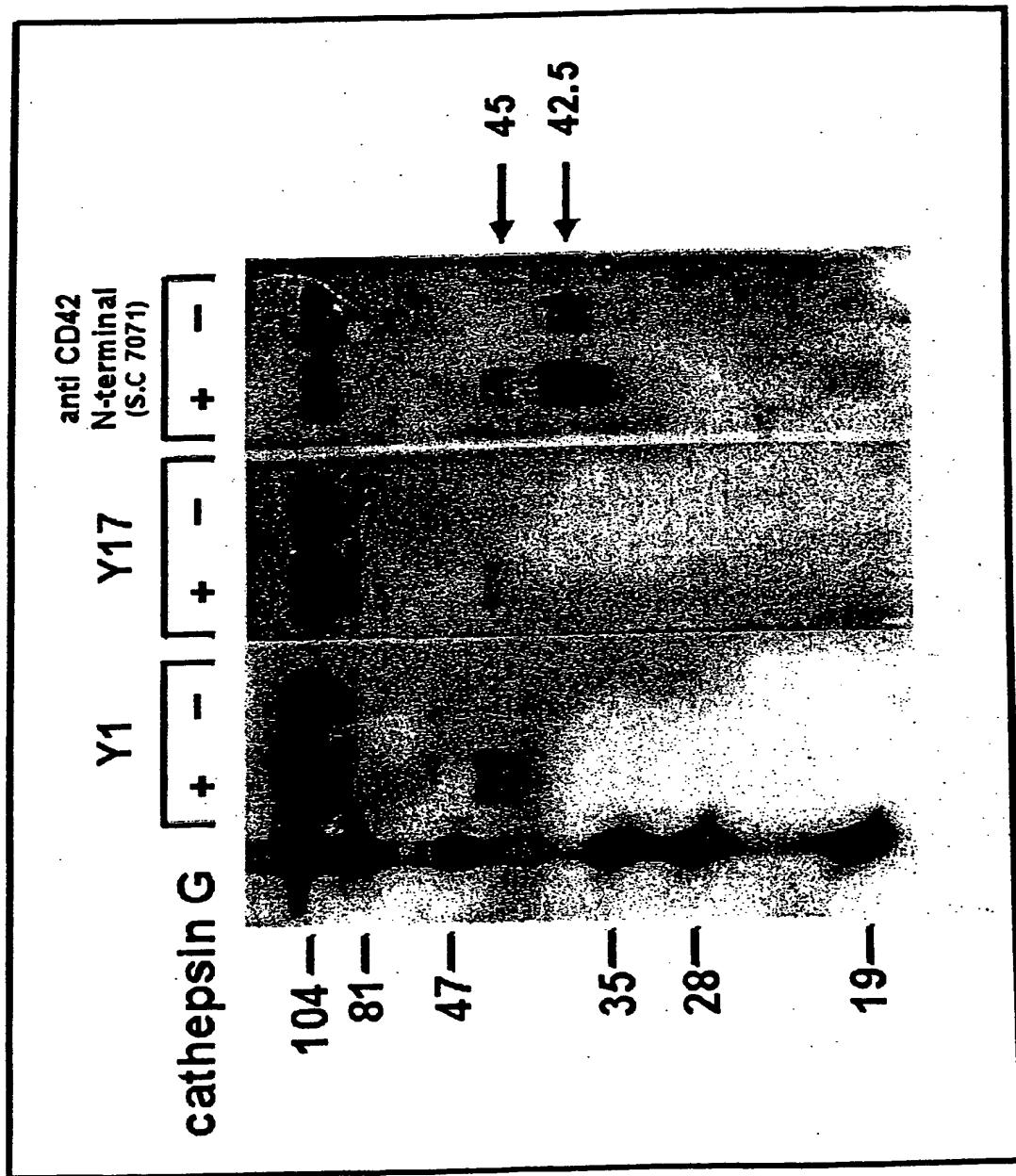




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FIG. 12

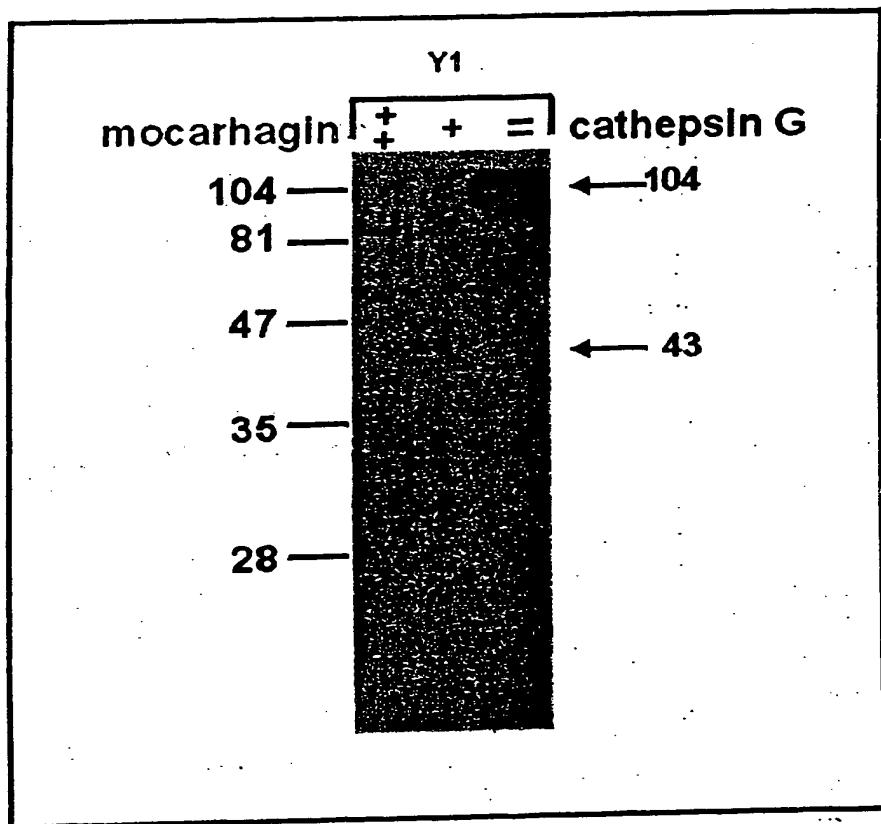
Y1 and Y17 reacts with larger cathepsin G cleaved platelets GPIb fragment





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FIG. 13

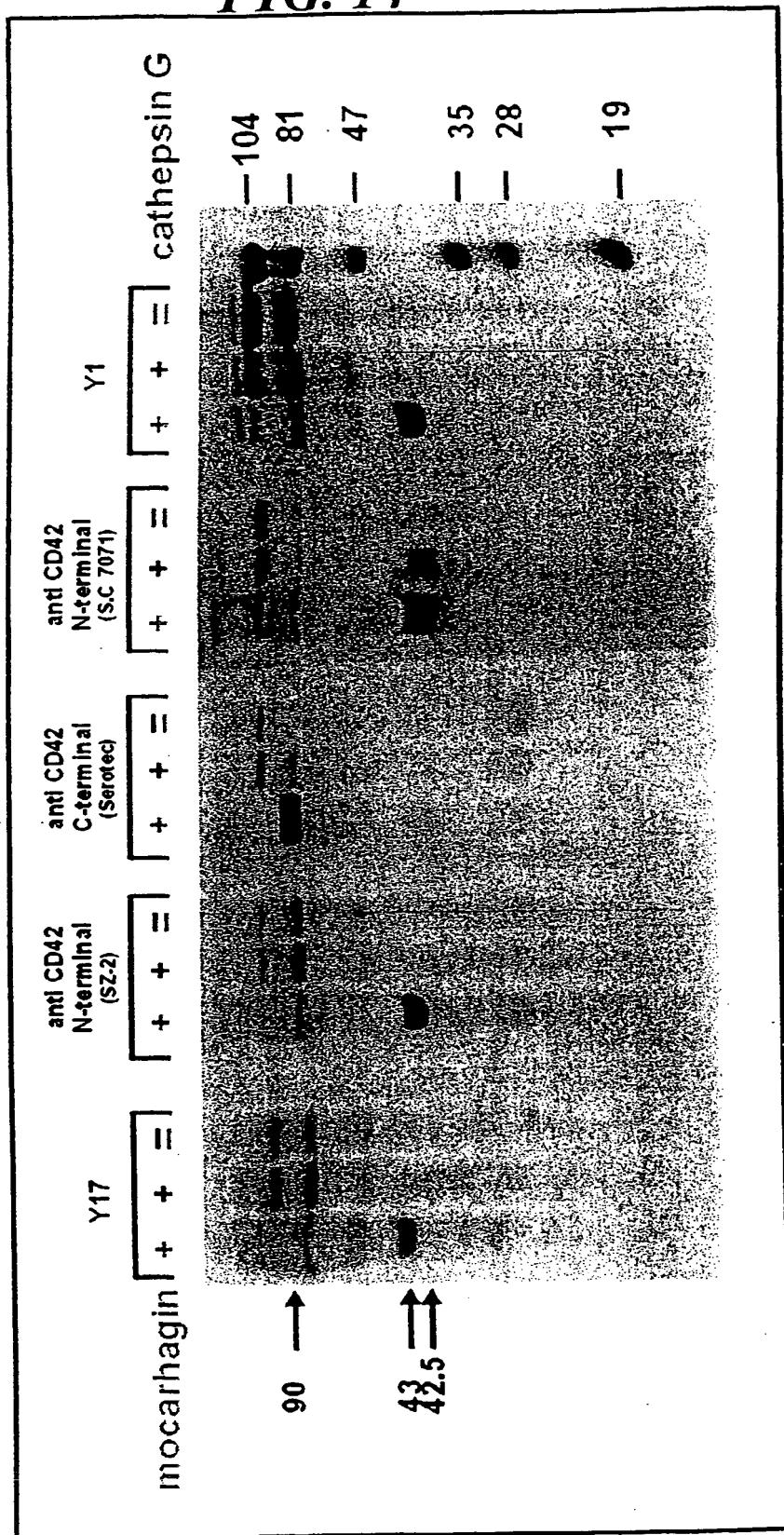




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Cleavage of washed platelets by mocarhagin and cathepsin G

FIG. 14

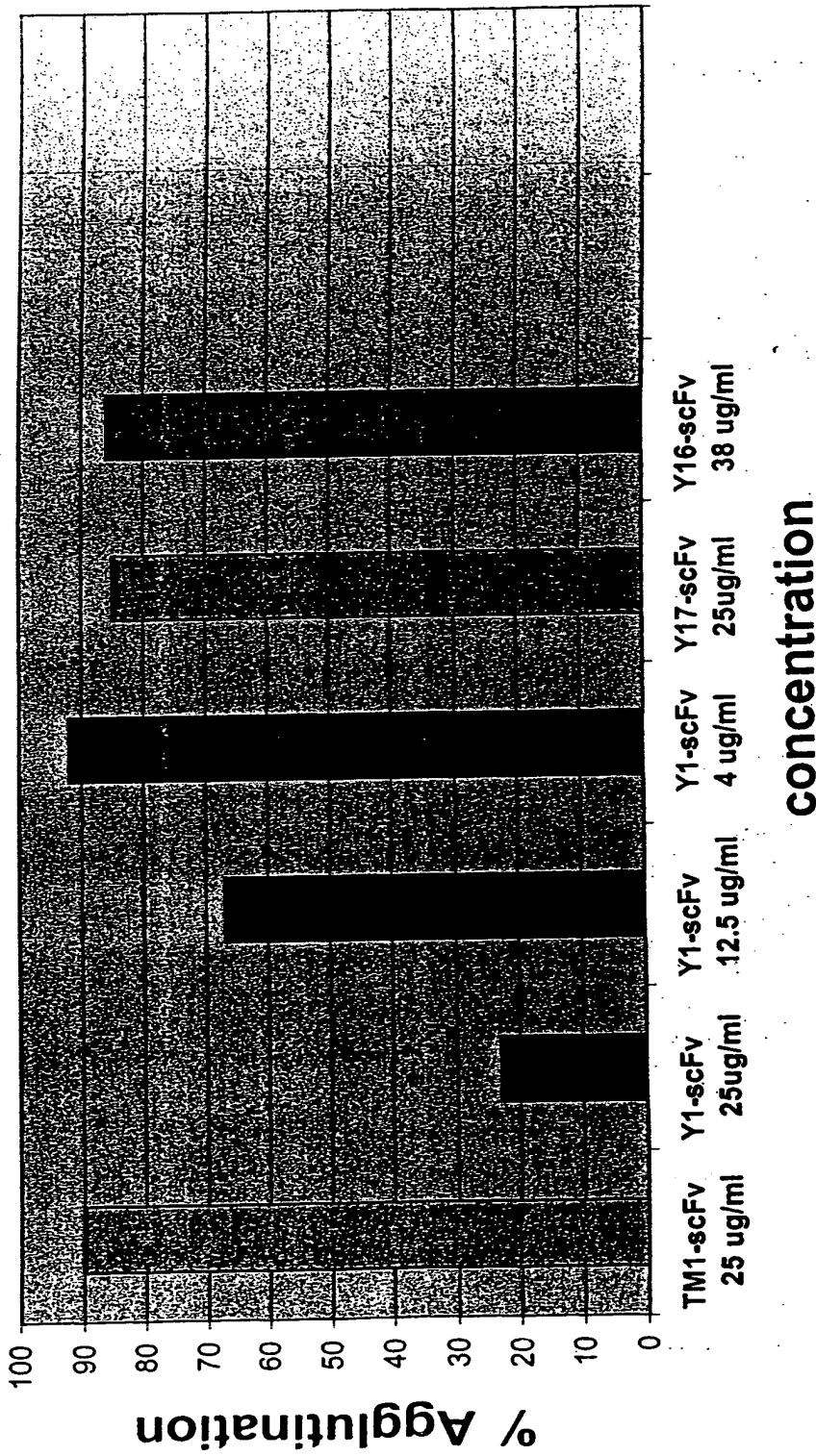


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FIG. 15

Influence of Y1-scFv on platelets agglutination in
washed platelets



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FIG. 16

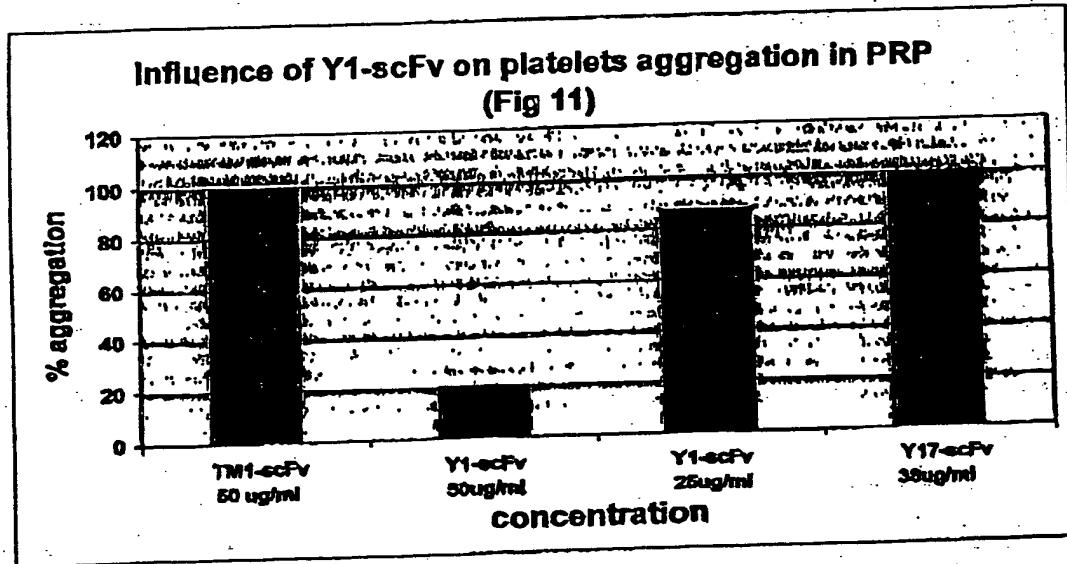
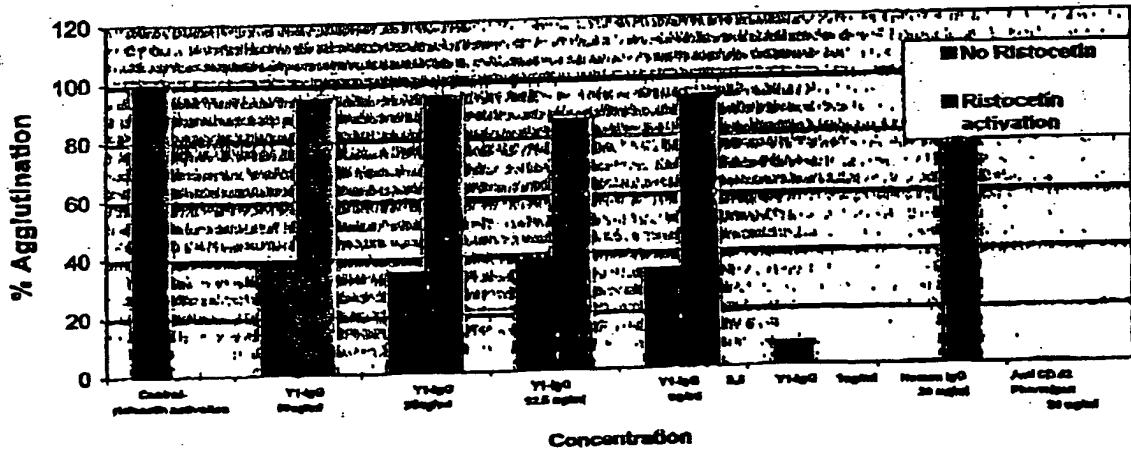




FIG. 17

Induction of platelet agglutination by Y1-IgG in washed platelets

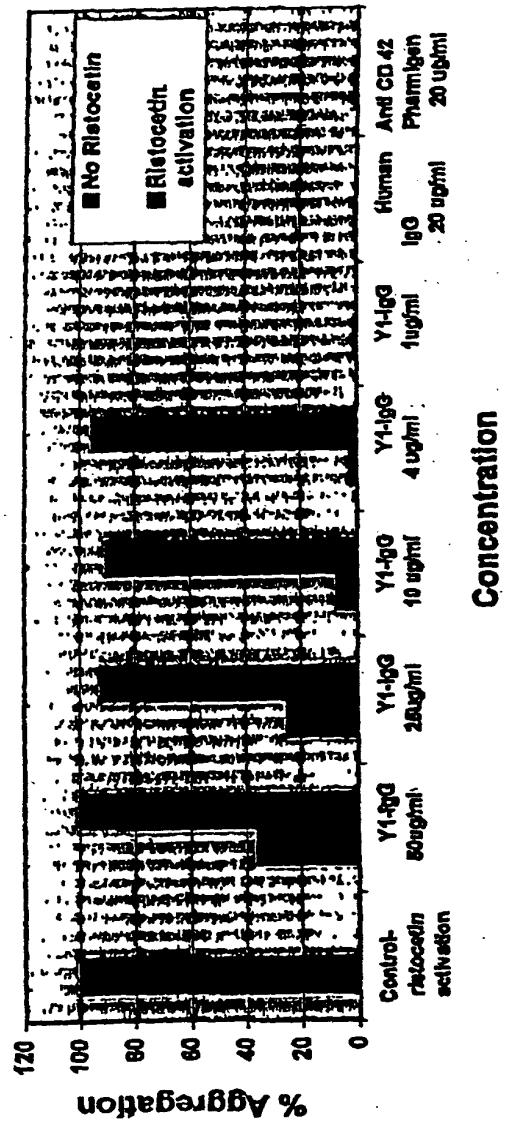




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FIG. 18

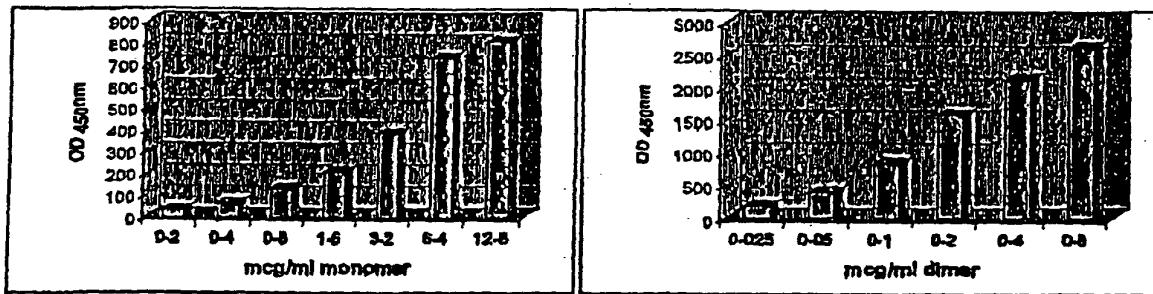
Induction of platelet aggregation by Y1-IgG in PRP





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FIG. 19





**Specificity of Binding of Y1
and α -CD42 (N1-19)
to their Ligands**

FIG. 20

181-B

Y1-B

α -CD42

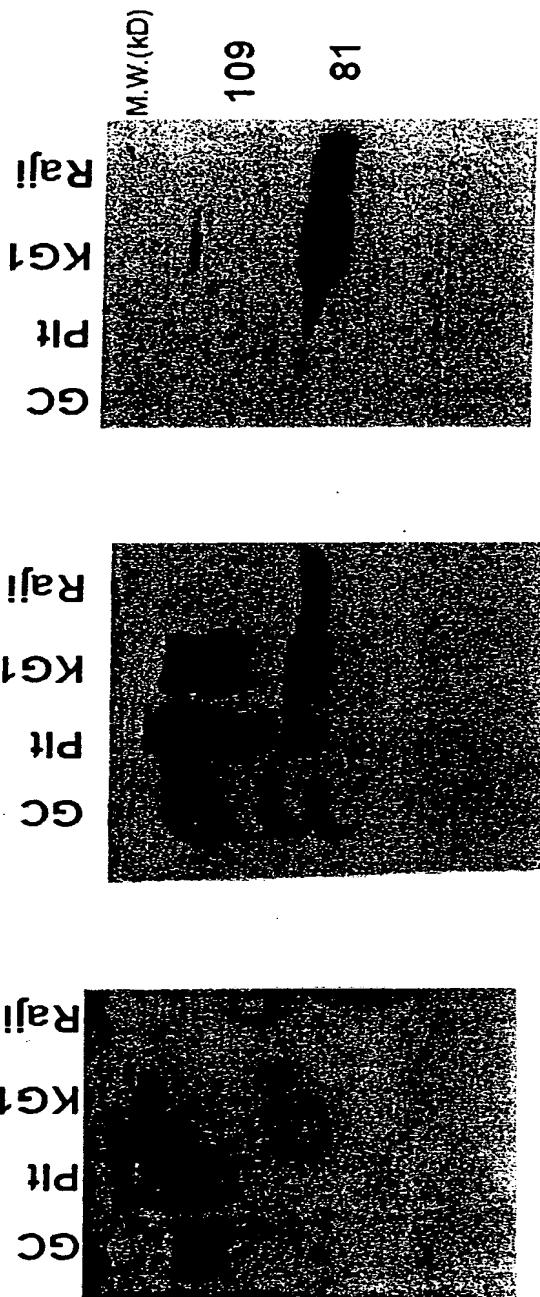
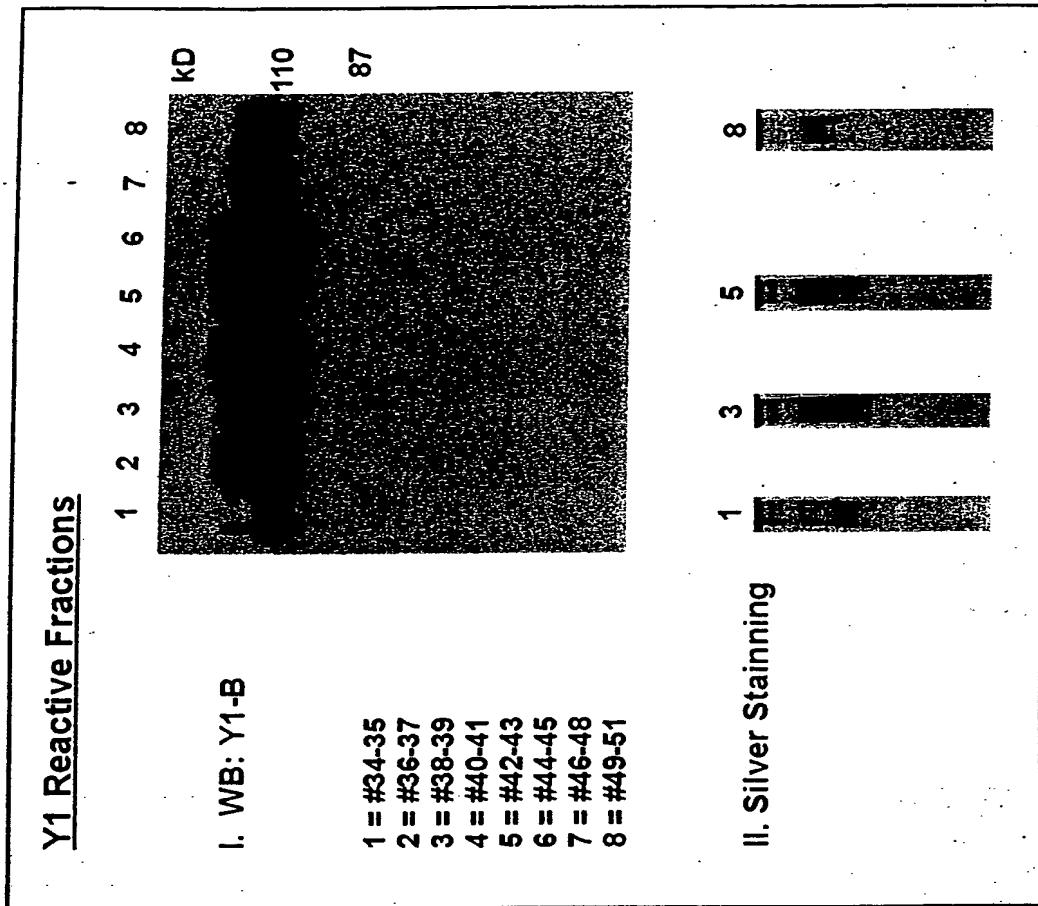




FIG. 21

**Y1-Ligand from KG1 membranes following
Immuno-Precipitation with Y1:
Purification on RP-HPLC**

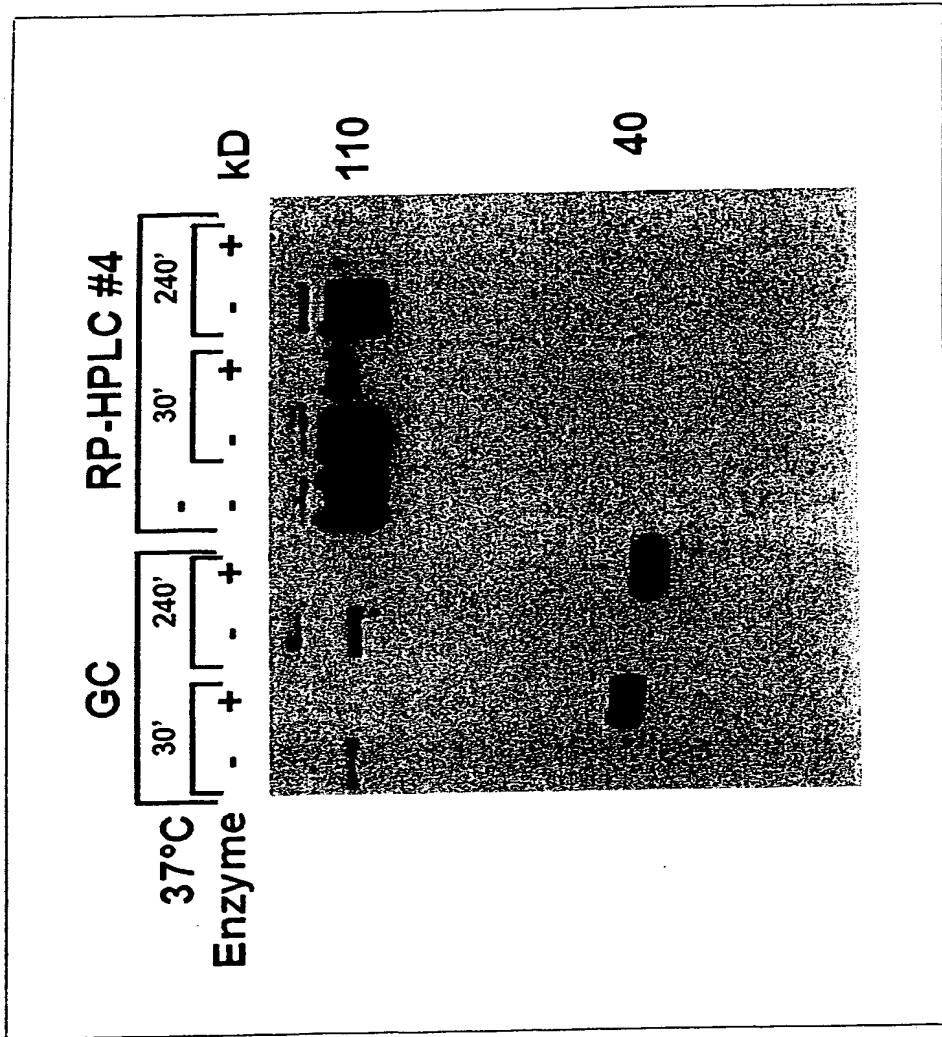


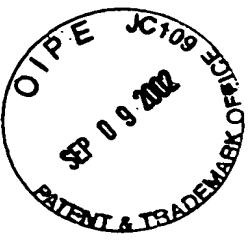


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FIG. 22

Effect of O-Sialo-Glycoprotein Endopeptidase on Y1 Binding

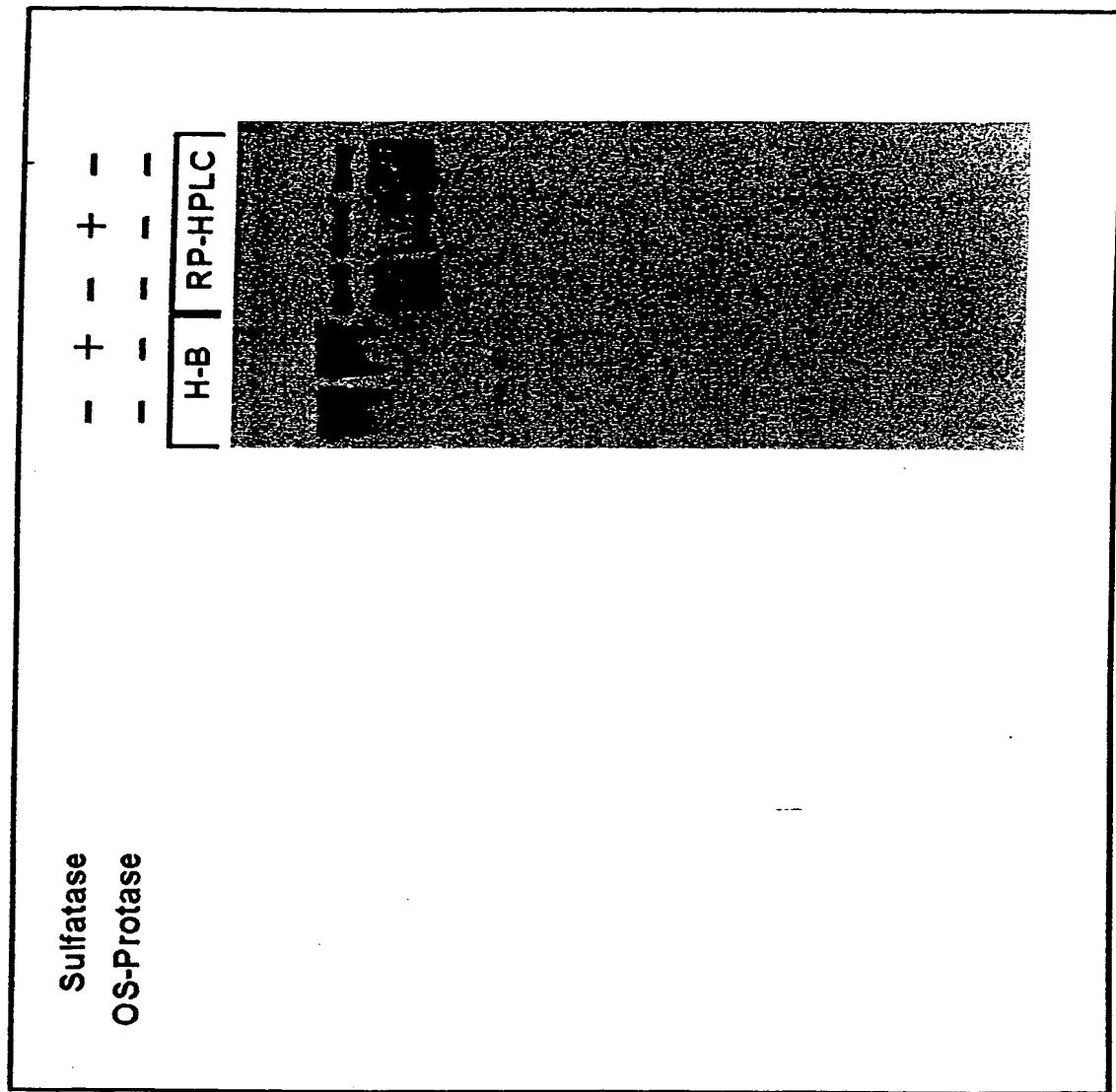




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FIG. 23

**Effect of Aryl-Sulfatase on Binding of Y1:
RP-HPLC(KG1) & H-B(Heparin-BSA)**

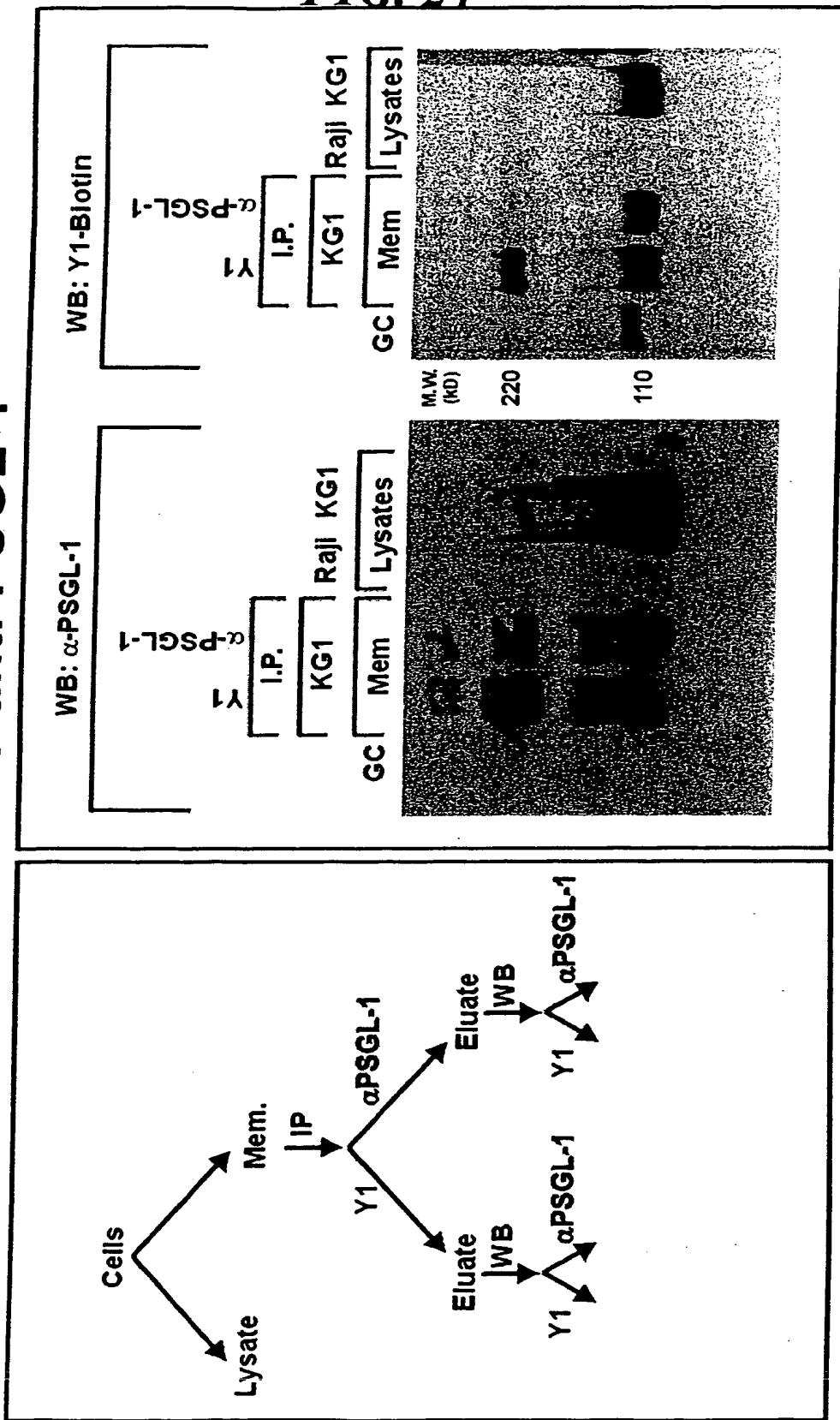




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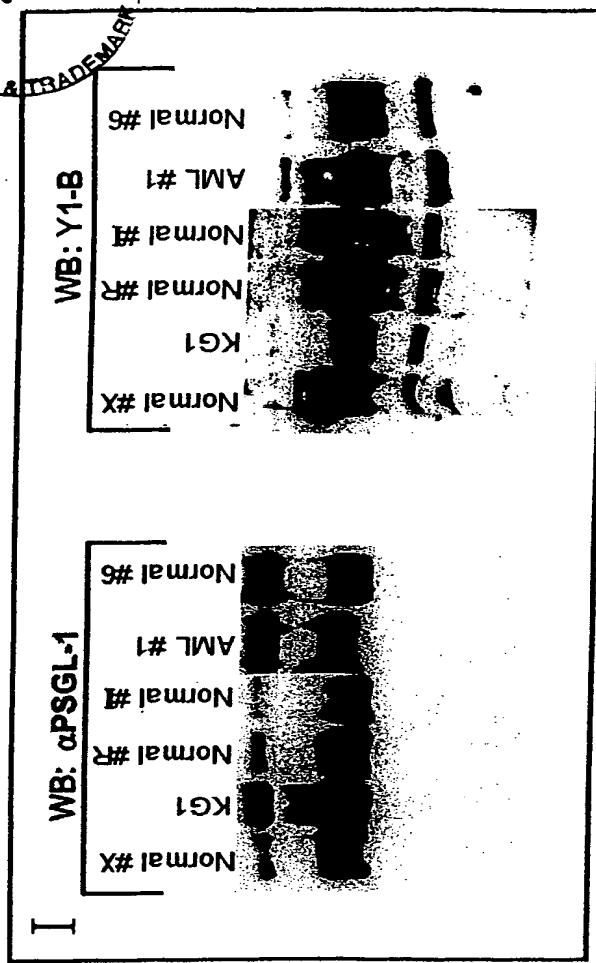
Specificity of Y1 Binding: Analysis by Immune Precipitation with Y1 and anti-PsGL-1

FIG. 24

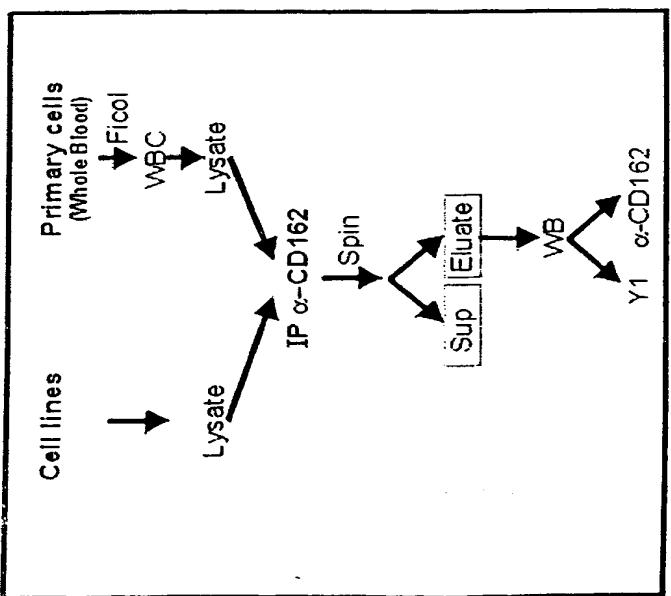
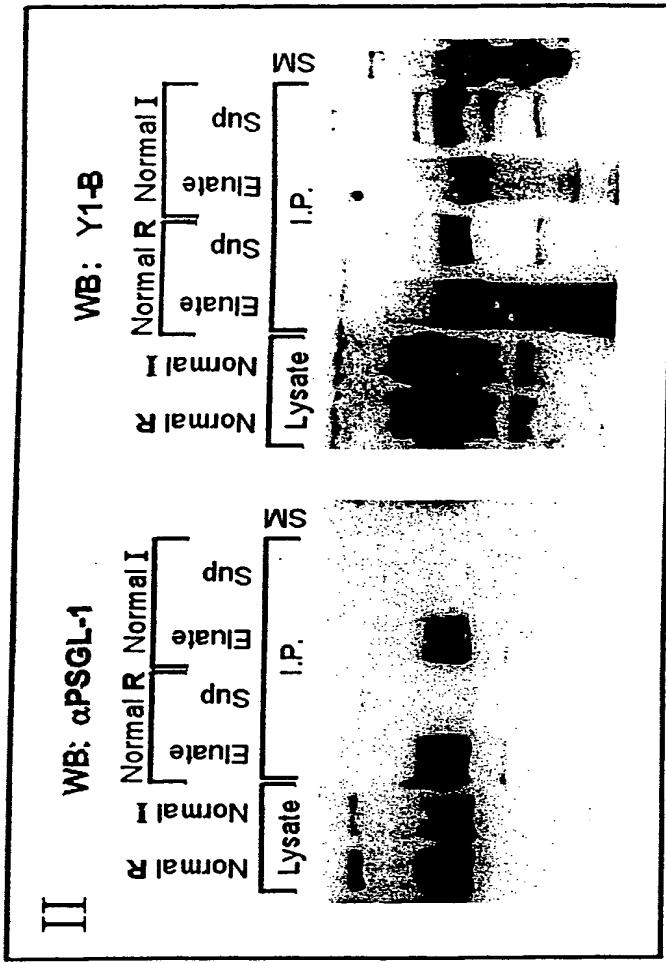


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FIG. 25



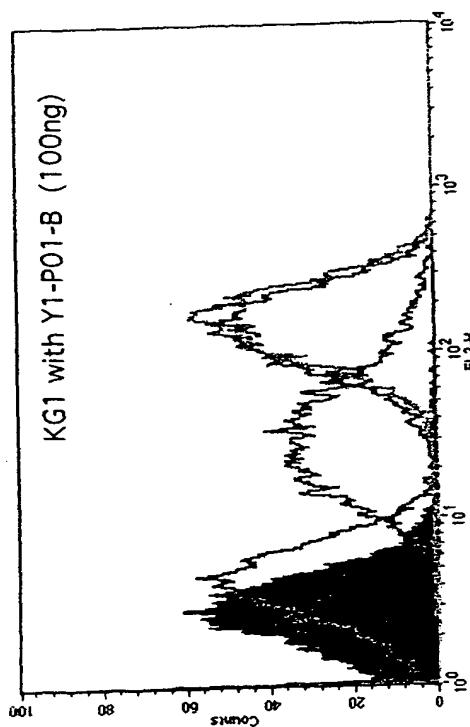
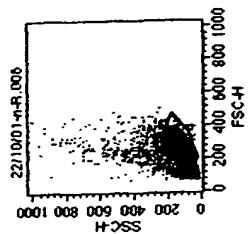
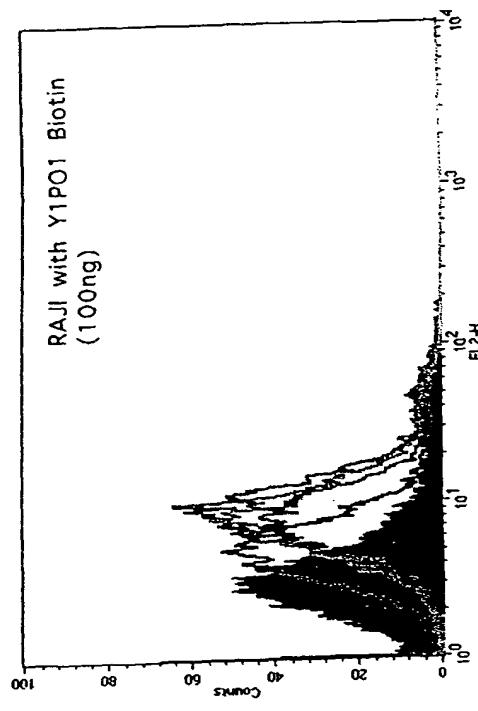
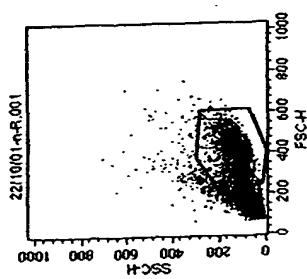
α -CD162 and Y1:
Comparison between cells
from AML patient and normal
blood





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FIG. 26



Key	Name	Parameter	Date
■	221/001-nR.006	N01-B	
■	221/001-nR.007	P01-B	
■	221/001-nR.008	+PL1	
■	221/001-nR.009	+PL1	
■	221/001-nR.010	+PL2	



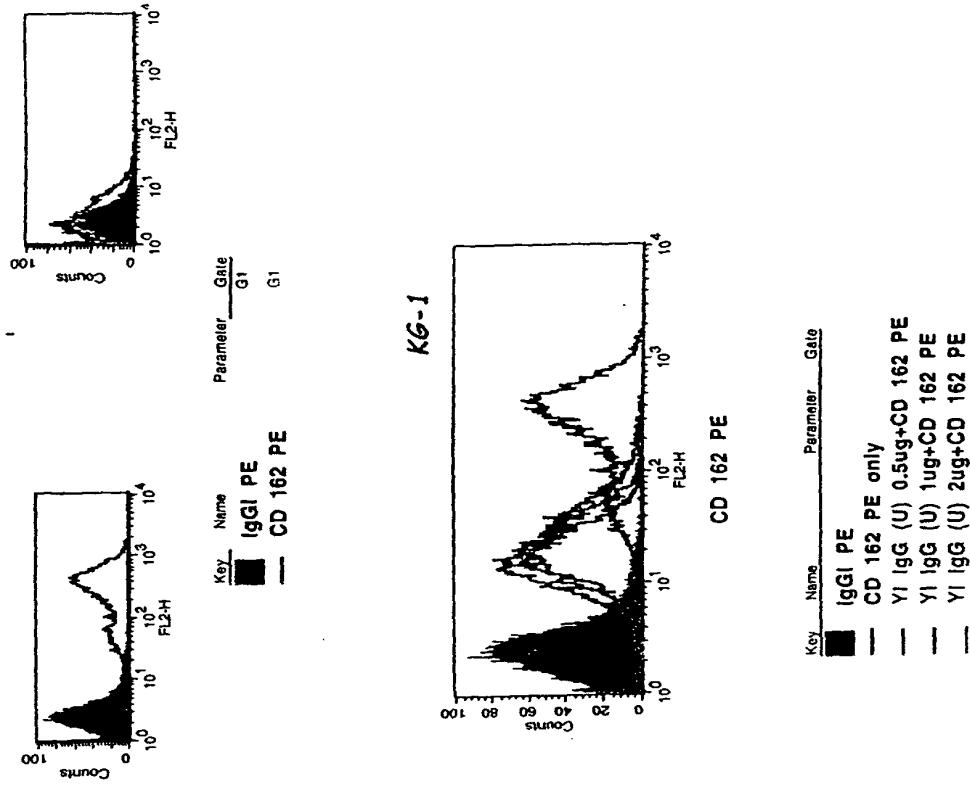
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FIG. 27

Specificity of Y1 Binding: Analysis by FACS

Raji

KG-1



- Binding of
 - α PSGL1
(αCD162/KPL1);
 - competition
 - with Y1-IgG

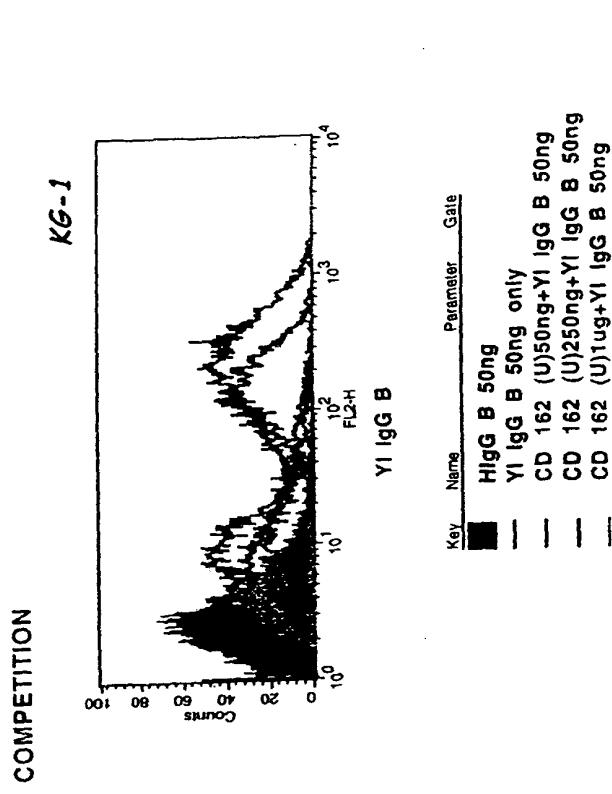


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FIG. 28

Specificity of Y1 Binding: Analysis by FACS

- Binding of Y1-IgG;
competition with α PSGL-1
(CD162 /KPL1)



COMPETITION

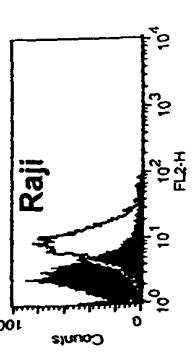
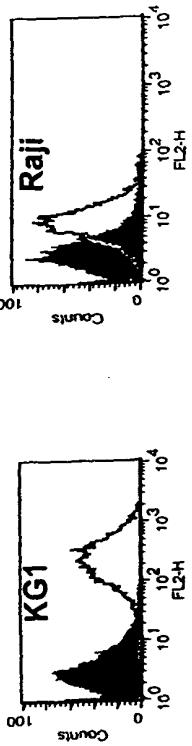
KG-1

Key Name Parameter Gate

Higg B 50ng
Y1 IgG B 50ng

G1 G1

+ SAV PE 1:100



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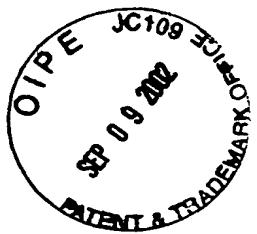
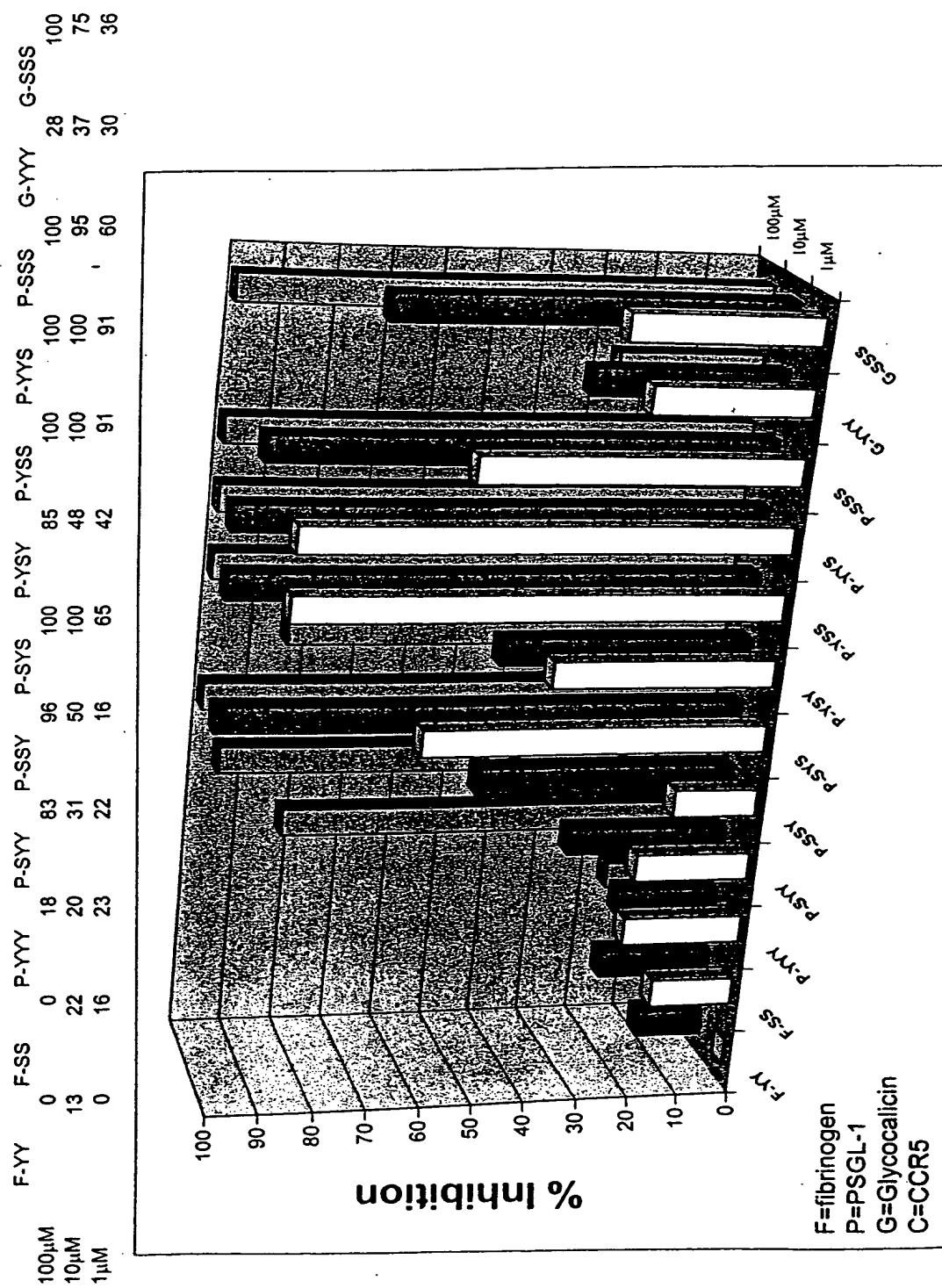


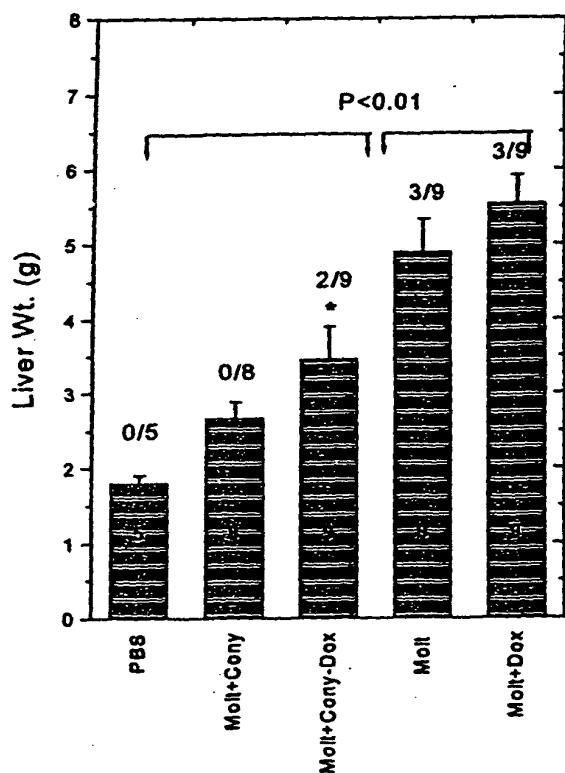
FIG. 29





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FIG. 30

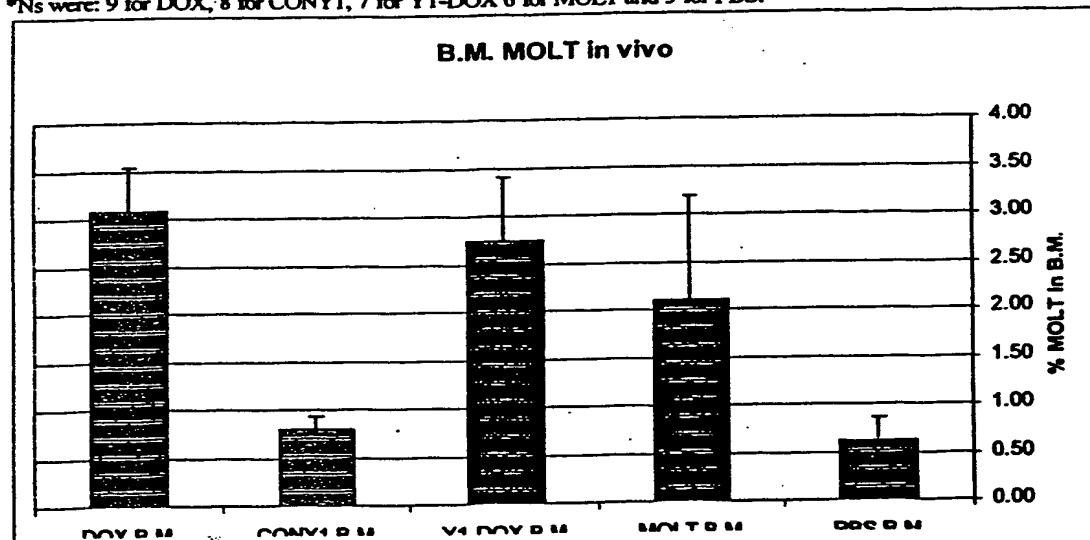




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FIG. 31

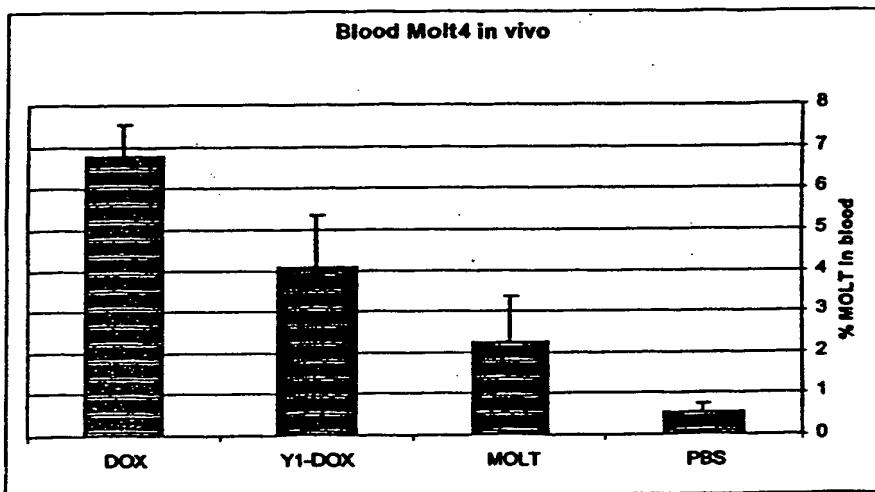
*Ns were: 9 for DOX, 8 for CONY1, 7 for Y1-DOX 6 for MOLT and 5 for PBS.





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FIG. 32

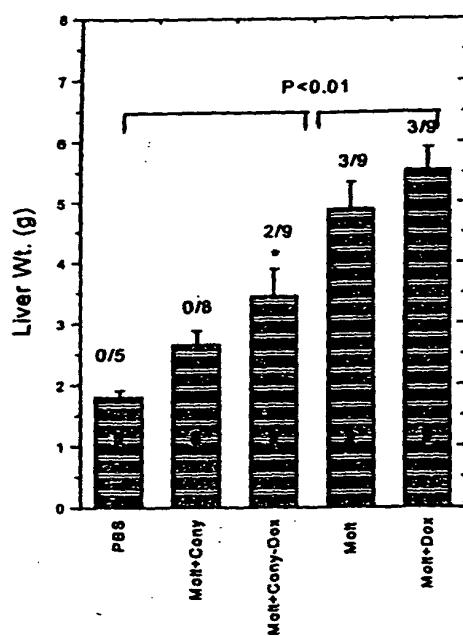


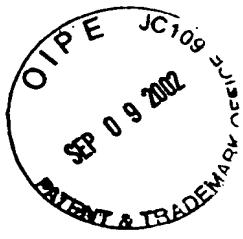
**Ns were: 4 for DOX, 2 for Y1-DOX, 3 for MOLT and 3 for PBS.

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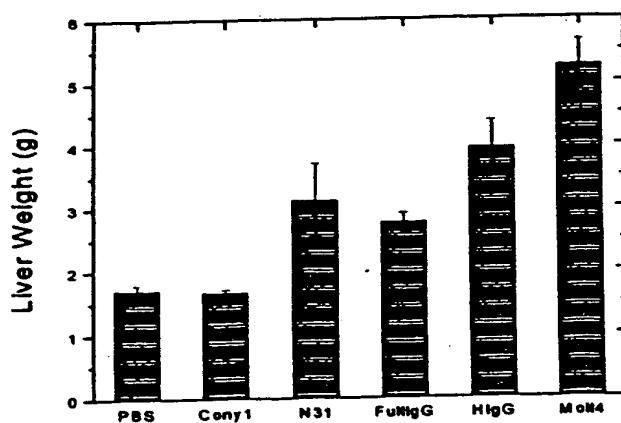
FIG. 33





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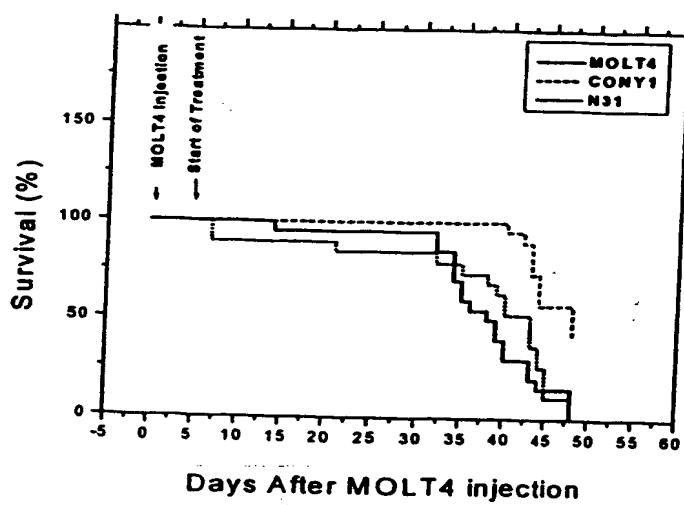
FIG. 34



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FIG. 35

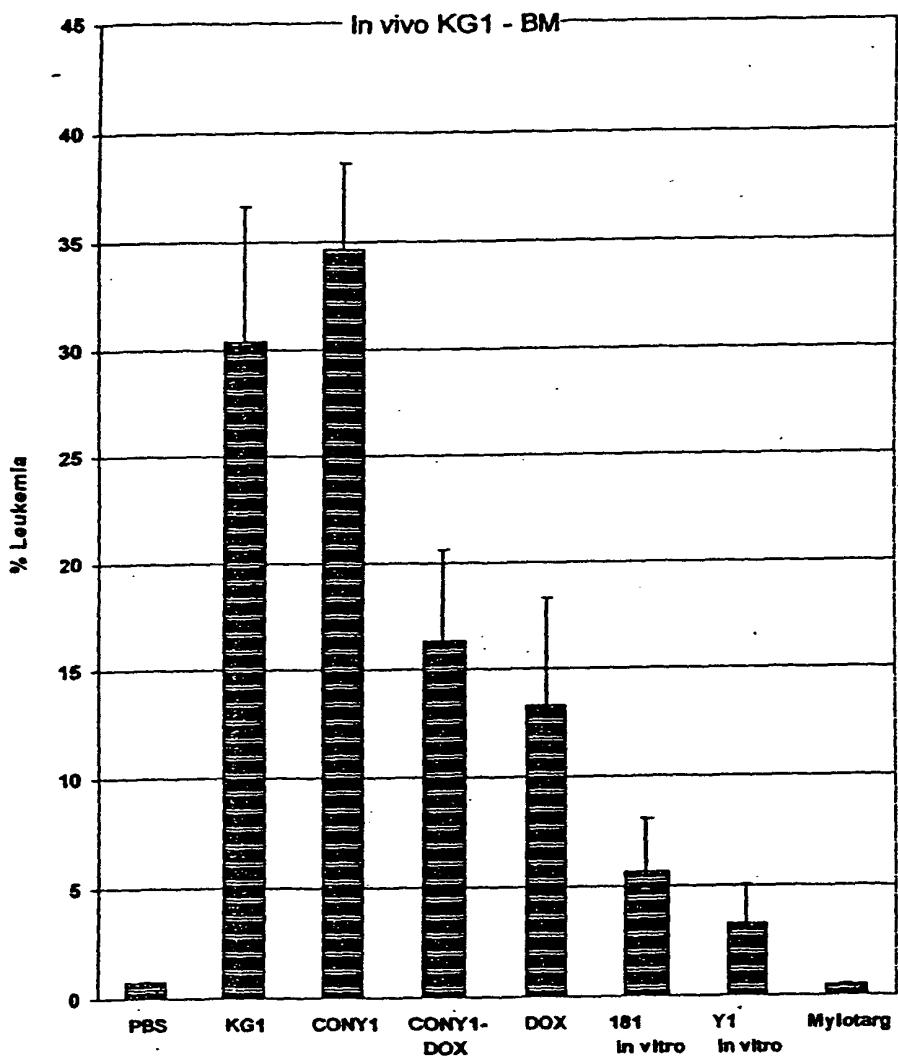


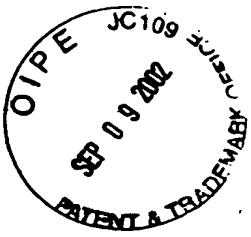


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FIG. 36

***Ns were: 8 for PBS, 9 for KG1, 8 for CONY1, 11 for CONY1-DOX, 9 for DOX, 8 for 181 in vitro, 9 for Y1 in vitro and 9 for Mylotarg.

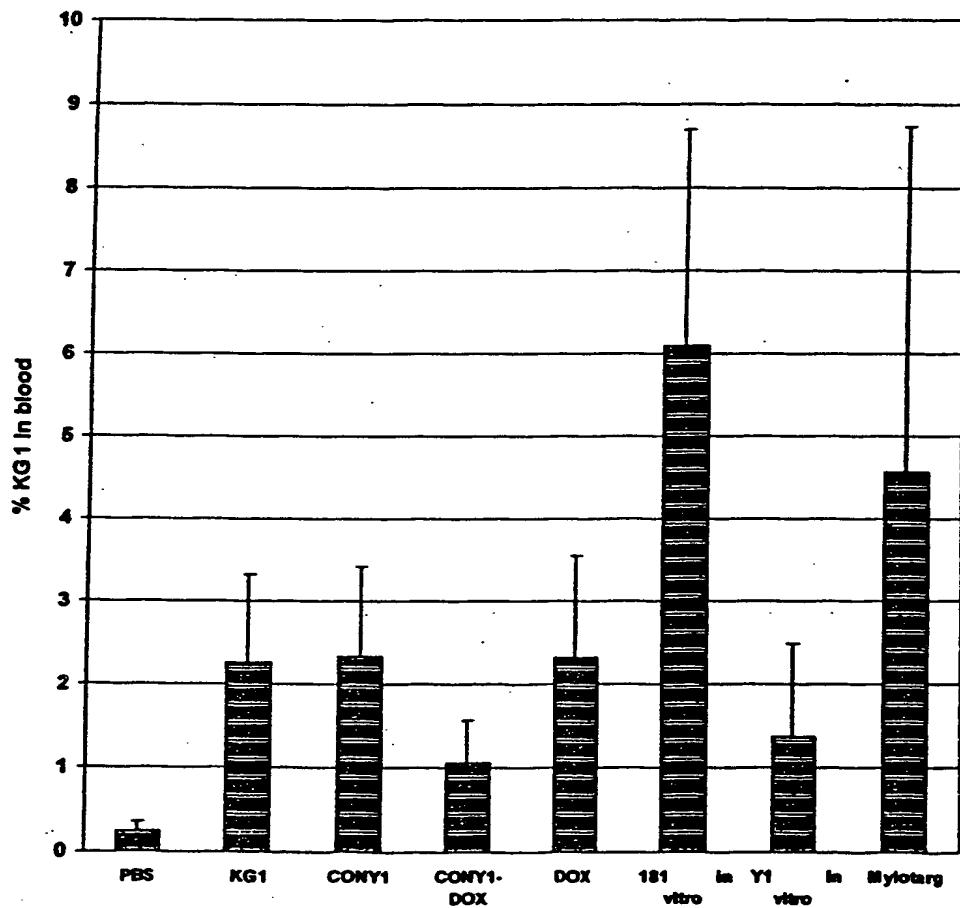




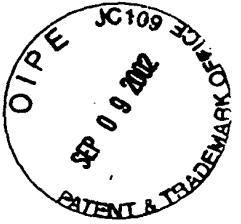
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FIG. 37

In vivo KG1 - Blood

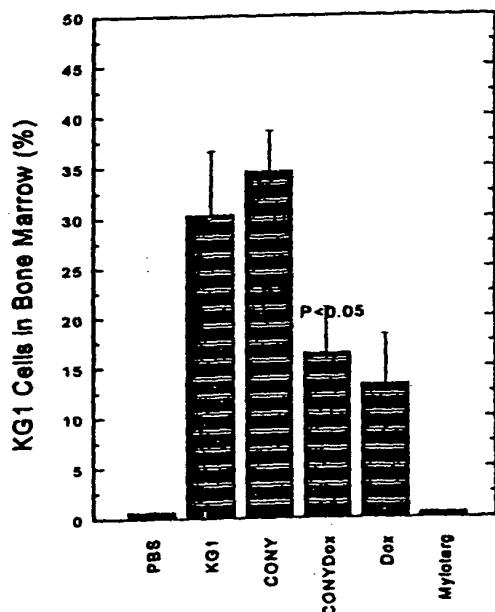


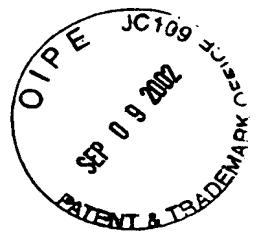
****Ns were: 8 for PBS, 9 for KG1, 8 for CONY1, 9 for CONY1-DOX, 11 for DOX (including one mice injected with 5mg/kg DOX), 7 for 181 in vitro, 8 for Y1 in vitro and 7 for Mylotarg.



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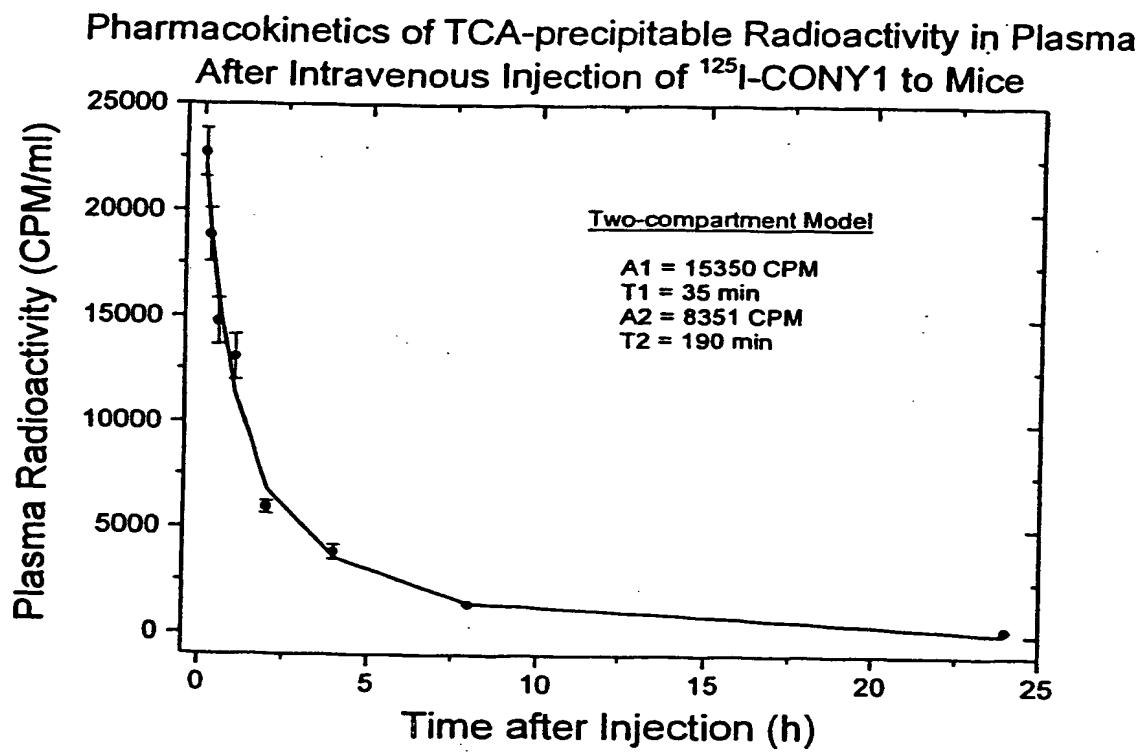
FIG. 38

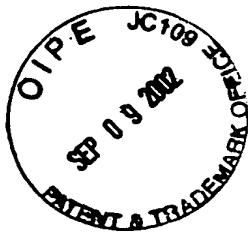




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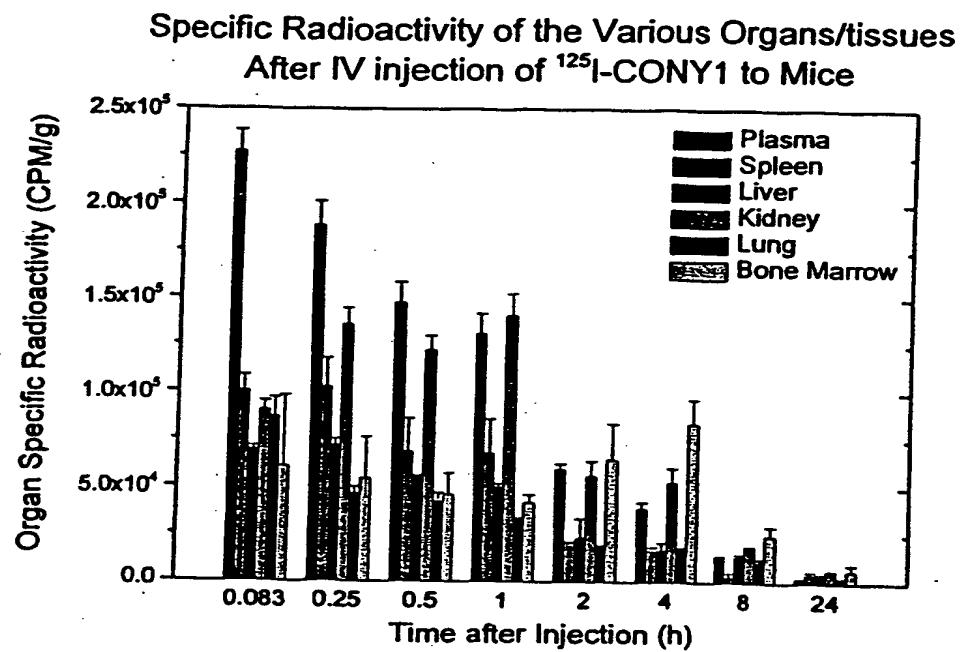
FIG. 39

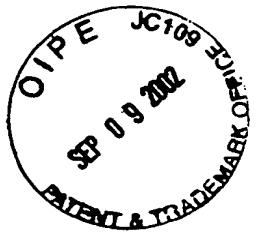




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FIG. 40

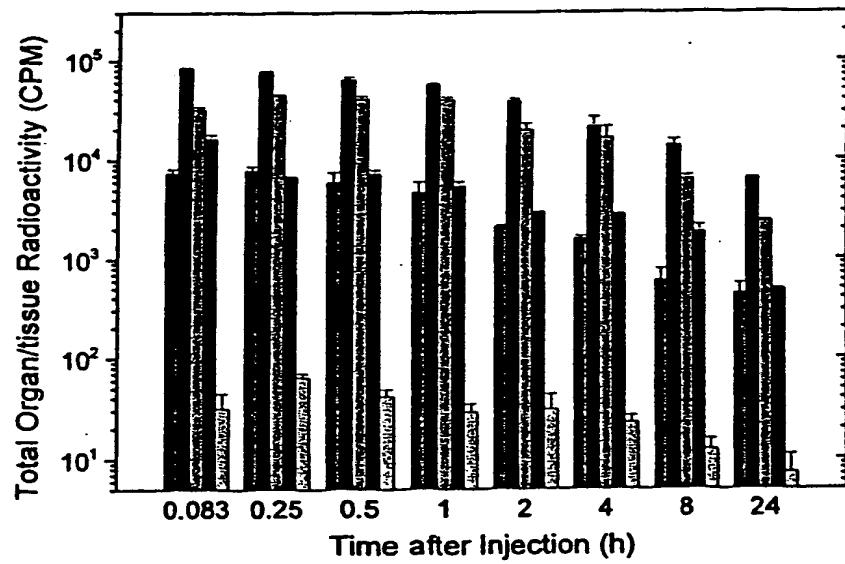


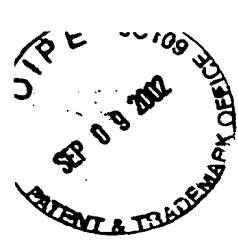


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FIG. 41

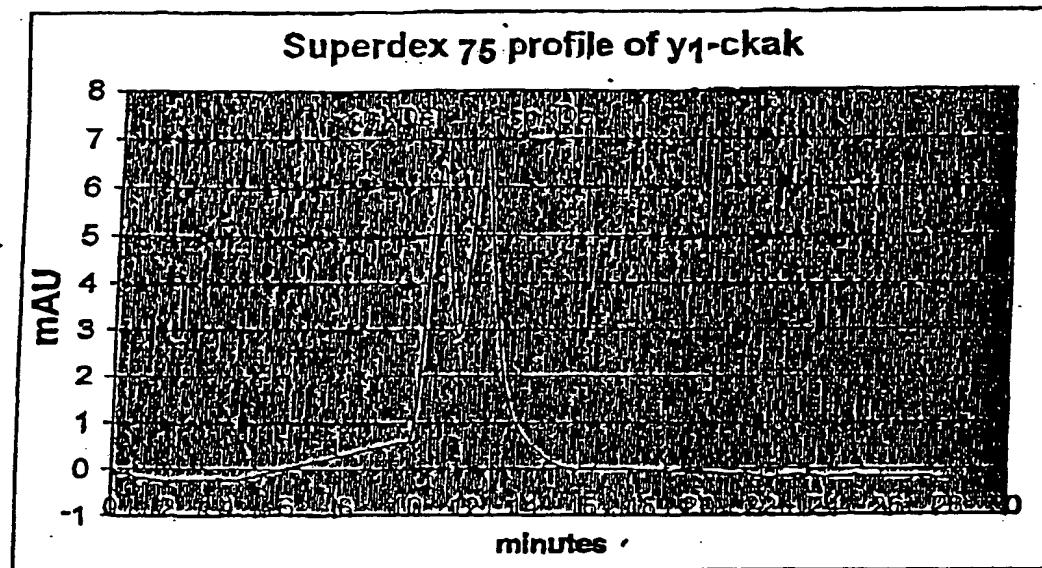
Distribution of Radioactivity in Body organs after
Injection of ^{125}I -CONY1 to Mice





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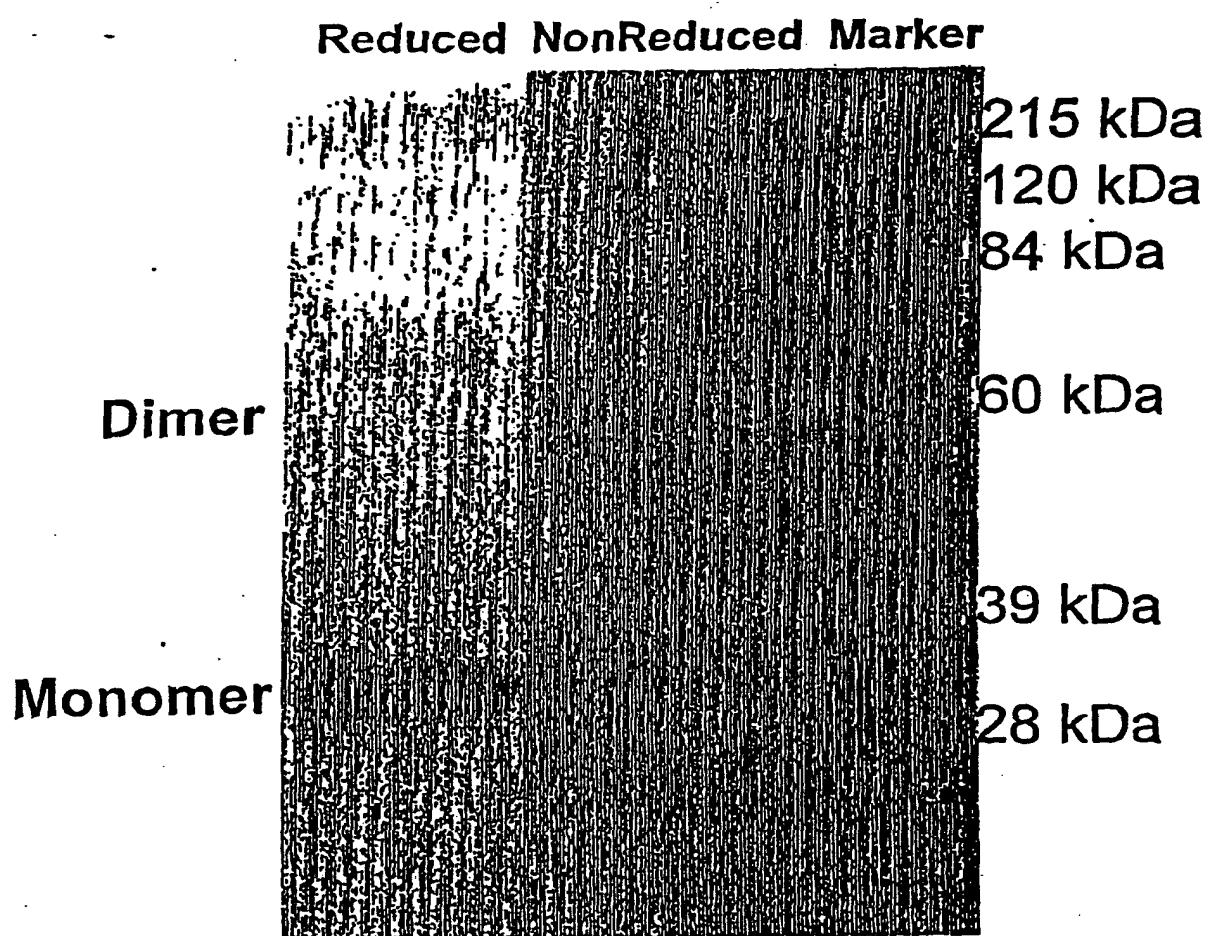
FIG. 42

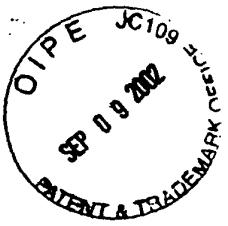




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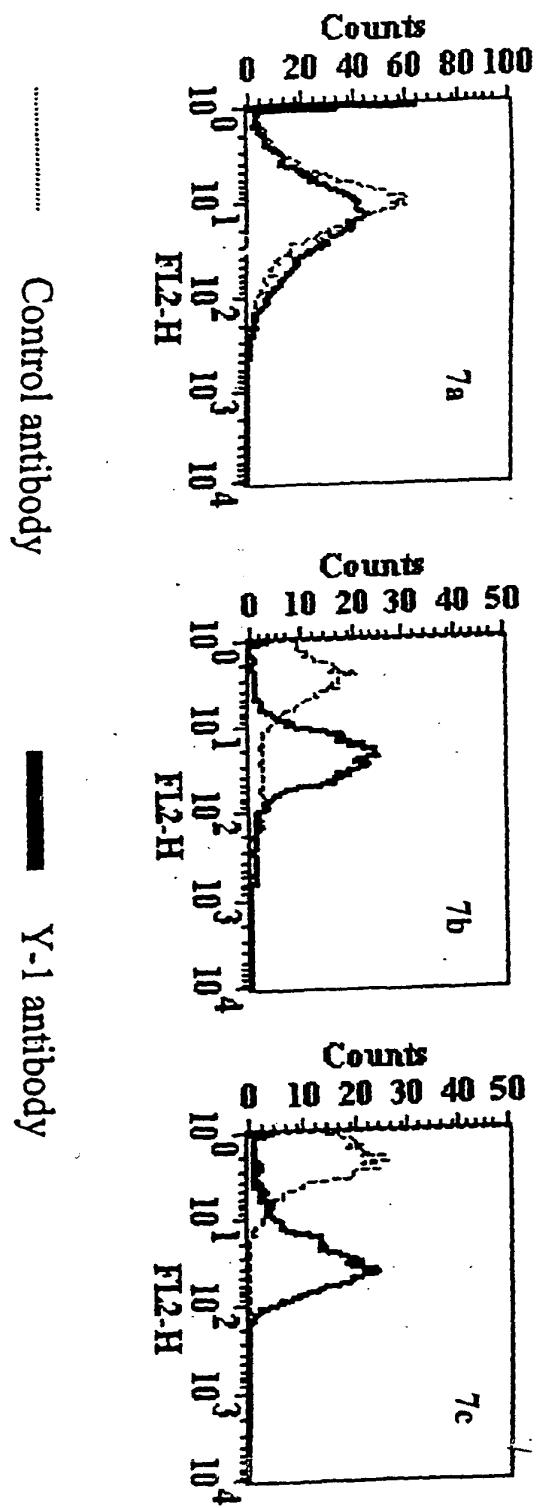
FIG. 43

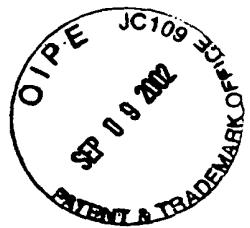




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FIG. 44

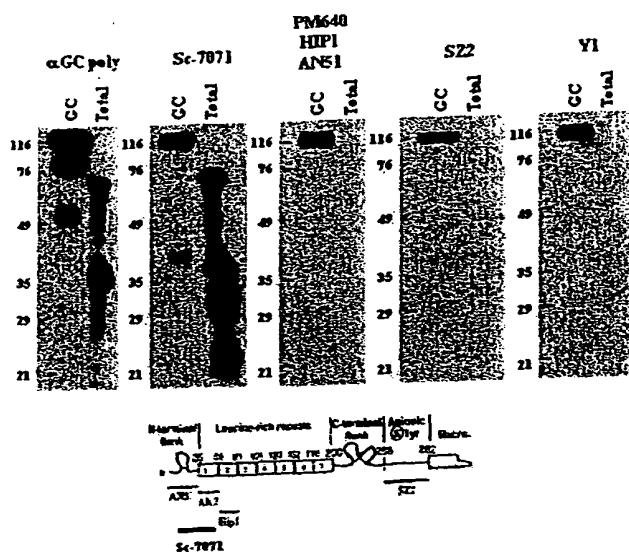


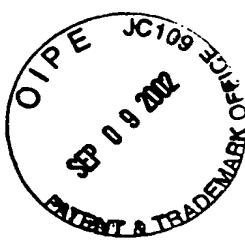


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FIG. 45

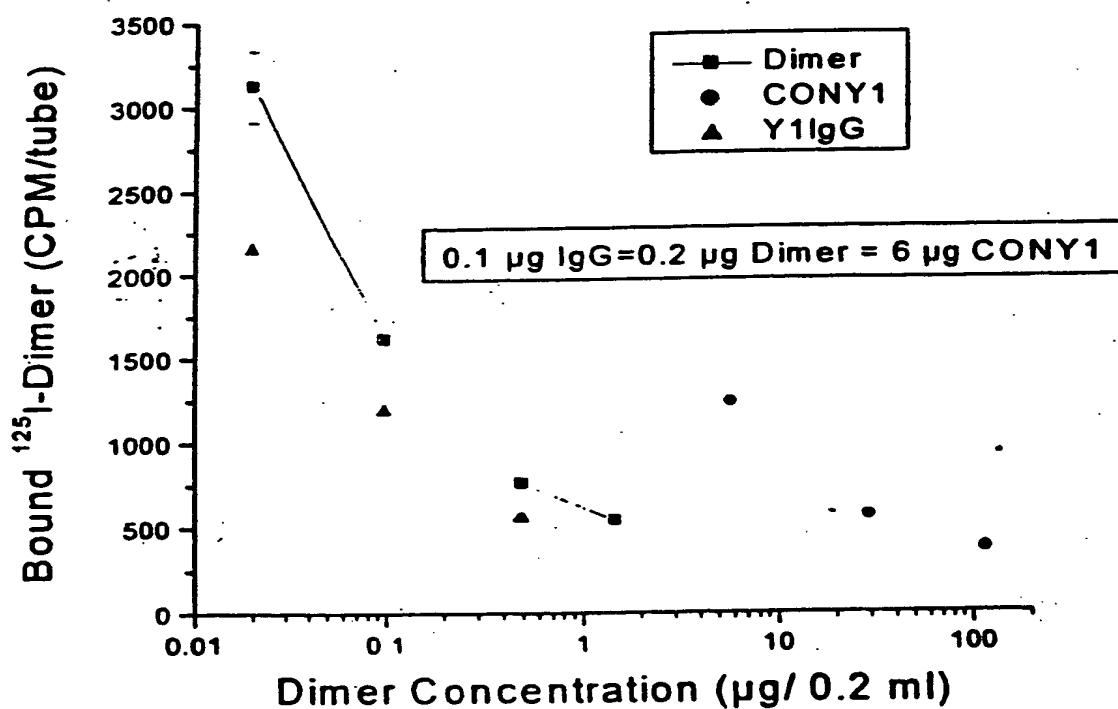
Epitopes of anti-GPI $\beta\alpha$ antibodies

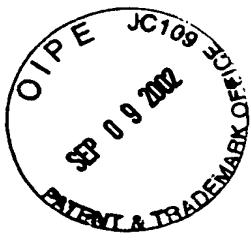




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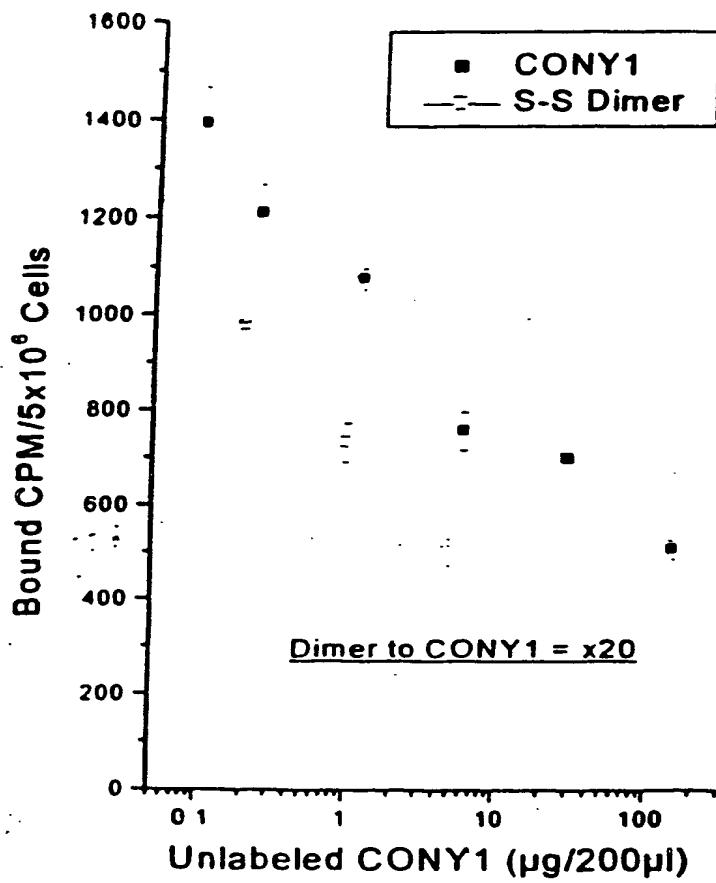
FIG. 46





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FIG. 47



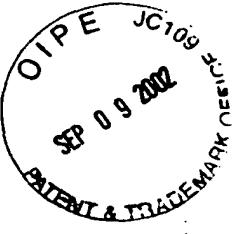
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FIG. 48A: The ORF and Amino Acid Sequence of Y1-HC

SEQ ID NO: 205 (nucleic acid sequence): SEQ ID NO: 206 (amino acid sequence)

1 ATGGCCCTGGGCTCTGCTGCCCTAACCTCCTCACTCAGGACACAGGGCCTGGCCGAT
1 M A W A L L L L T L L T Q D T G S W A D
61 ATCCAGCTGGTGGAGTCTGGGGAGGTGTGGTACGGCCTGGGGGTCCTGAGACTCTCC
21 I Q L V E S G G G V V R P G G S L R L S
121 TGTCAGCCTCTGGATTCACCTTGATGATTATGGCATGAGCTGGTCCGCCAAGCTCCA
41 C A A S G F T F D D Y G M S W V R Q A P
181 GGGAAAGGGCTGGAGTGGTCTGGTATTAAATTGGAATGGTGGTAGCACAGGTTATGCA
61 G K G L E W V S G I N W N G G S T G Y A
241 GACTCTGTGAAGGGCGATTCACCATCTCTAGAGACAACGCCAAGAACCTCCCTGTATCTG
81 D S V K G R F T I S R D N A K N S L Y L
301 - 301 - CAAATGAACAGTCTGAGAGCCGAGGGACACGGCGTGTATTACTGTGCAAGAACATGAGGGCT
101 Q M N S L R A E D T A V Y Y C A R M R A
361 CCTGTGATTTGGGCCAAGGTACCCCTGGTCACCGTCTCGAGTGTGCTTCCACCAAGGGCCA
121 P V I W G Q G T L V T V S S A S T K G P
421 TCGGTCTCCCCCTGGCACCCCTCCAAGAGCACCTCTGGGGCACAGCGGCCCTGGC
141 S V F P L A P S S K S T S G G T A A L G
481 TGCCTGGTCAAGGACTACTTCCCCGAACCGGTACGGTGTGGAACTCAGGCCCTG
161 C L V K D Y F P E P V T V S W N S G A L
541 ACCAGCGCGTGCACACCTTCCCCGTGCTCACAGTCCTCAGGACTCTACTCCCTCAGC
181 T S G V H T F P A V L Q S S G L Y S L S
601 AGCGTGGTGACCGTGGCCCTCCAGCAGCTGGGACCCAGACCTACATCTGCAACGTGAAT
201 S V V T V P S S S L G T Q T Y I C N V N
661 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCAAATCTTGTGACAAA
221 H K P S N T K V D K R V E P K S C D K T
721 CACACATGCCACCCTGCCCCAGCACCTGAACCTCTGGGGGACTGTCAGTCCTCOTCTTC
241 H T C P P C P A P E L L G G P S V F L F
781 CCCCCAAAACCCAAGGACACCCCTCATGATCTCCGGACCCCTGAGGTACATGCGTGGT
261 P P K P K D T L M I S R T P E V T C V V
841 GTGGACGTGAGCCACCGAAGACCCCTGAGGTCAAGTCACTGGTACGTGGACGGCGTGGAG
281 V D V S H E D P E V K F N W Y V D G V E
901 GTGCATAATGCCAAGACAAAGCCGGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
301 V H N A K T K P R E E Q Y N S T Y R V V
961 AGCGTCCTACCGTCTGCCAGCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTC
321 S V L T V L H Q D W L N G K E Y K C K V
1021 TCCAACAAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCC
341 S N K A L P A P I E K T I S K A K G Q P
1081 OGAGAACACAGGTGTACACCCCTGGCCCCATCCCGGAGGGAGATGACCAAGAACAGGTC
361 R E P Q V Y T L P P S R E E M T K N Q V
1141 AGCCTGACCTGGCTCAAAGGCTTCTATCCAGCGACATGCCGTGGAGTGGAGAG
381 S L T C L V K G F Y P S D I A V E W E S
1201 AATGGGCAGCCGGAGAACAACTACAAGACCACTGGCTCCCGTGTGGACTCCGACGGCTCC
401 N G Q P E N N Y K T T S P V L D S D G S
1261 TTCTTCCTCTATAGCAAGCTACCGTGCACAGGAGCAGGTGGCAGCAGGGAAACGTCTTC
421 F F L Y S K L T V D K S R W Q Q G N V F
1321 TCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACCGCAGAAGAGCCTCTCCCTG
441 S C S V M H E A L H N H Y T Q K S L S L
1381 TCTCTGGTAAATGA
461 S L G K *



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FIG. 48B: The ORF and Amino Acid Sequence of Y1-LC

SEQ ID NO: 207 (nucleic acid sequence); SEQ ID NO: 208 (amino acid sequence)

1 ATGGCCTGGGCTCTGCTGCTCCCTACCCCTCCACTCAGGACACAGGGCTGGGCCGAT
1 M A W A L L L T L L T Q D T G S W A D

61 GCAGAGCTGACTCAGGACCCCTGCTGTGTCTGTGGCCTGGACAGACAGTCAGGATCACA
21 A E L T Q D P A V S V A L G Q T V R I T

1212 TGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACCAGCAGAACGCCAGGACAG
41 C Q G D S L R S Y Y A S W Y Q Q K P G Q

181 GCCCCCTGTACTTGTCATCTATGGAAAAACAACCGGCCCTCAGGGATCCCAGACCGATTG
161 A P V L V I Y G K N N R P S G I P D R F

241 TCTGGCTCCAGCTCAGGAAACACAGCTTCCCTGACCATCACTGGGGCTCAGGCCGAAGAT
81 S G S S S G N T A S L T I T G A Q A E D

301 GAGGCTGACTATTACTGTAACCTCCGGGACAGCAGTGGTAACCATGTGGTATTCCGGGA
101 E A D Y Y C N S R D S S G N H V V F G G

361 GGGACCAAGCTGACCGTCCCTAGGTCAAGCCAAGGCCACACTGGTGTCTCATAGTGACTTC
121 G T K L T V L G Q P K A A P S V T L F P

421 CCCTCCTCTGAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTCTCATAGTGACTTC
141 P S S E E L Q A N K A T L V C L I S D F

481 TACCCGGGAGCCGTGACAGTGGCTGGAAAGGCAGATAGCAGCCCGTCAAGGCCGGAGTG
161 Y P G A V T V A W K A D S S P V K A G V

541 GAGACCACACACCCCTCAAACAAAGCAACAACAAGTACGCCAGCAGCTACCTGAGC
181 E T T T P S K Q S N N K Y A A S S Y L S

601 CTGACGCCCTGAGCAGTGGAAAGTCCCACAAAAGCTACAGCTGCCAGGTACGCATGAAGGG
201 L T P E Q W K S H K S Y S C Q V T H E G

661 AGCACCGTGGAGAAGACAGTGGCCCTACAGAATGTTCATGA
221 S T V E K T V A P T E C S *

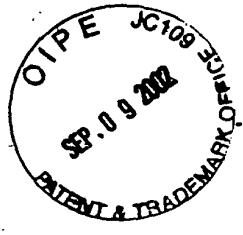
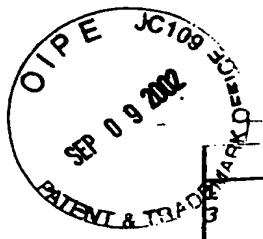


FIG. 49

	11	21	31	41	51	
1						
61	EVQLVESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVA ISGSGGSTYY 60					
121	ADSVKGRFTI SRDNSKNTLY LQMNLSRAED TAVYYCARVA KTLMRQYSIW GQGTLVTVSR 120					
181	GGGGSGGGGS GGGGSSELTQ DPAVSVALGQ TVRITCQGDS LRSYYASWYQ QKPGQAPVLV 180					
241	IYGKNVRPSG IPDRFSGSSS GNTASLTITG AQAEDeadYY CNSRDSSGNH VVFGGGTKL 240					
	VLGAAAEEQKL ISEEDLNAA					

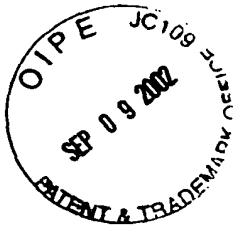


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FIG. 50

	10	20	30	40	50	60
	A t T A T T A C T C	g C G G G C C A G C	C g G C C A G C	C G A G G T G C A G	C T G G T G G A G T	C T G G G G G A G G
	L L L A A Q P A M	A F K E	V Q	L V E	S G G G	G
	70	80	90	100	110	120
1	C T I G G T A C A G	C C T G G G G G T	C C C T G A G A C T	C T C C T G T G C A	G C C T C T G G A T	T C A C C T T T A G
3	L V Q P G G S L R L	S L R L	S C A A S G	F T F S		
	130	140	150	160	170	180
1	C A G C T A T G C C	A T G A G C T G G G	T C C G C C A G G C	T C C A G G G A A G	G G G C T G G A G T	G G G T C T C A C G C
3	S Y A M S W V R Q A	P G K G L E	W V S A			
	190	200	210	220	230	240
1	T A T T A G T G G T	A G T G C T G G T A	G C A C A T A C T A	C C C A G A C T C C	G T G A A G G G C C	G G T T C A C C A T
3	I F S G S G G S T Y Y	A D S V K G	R F T I			
	250	260	270	280	290	300
1	C T C C A G A G A C	A A T T C C A A G A	A C A C G C T G T A	T C T G C A A A T G	A A C A G C C T G A	G A G C C G A G G A
3	S R D N S K N T L Y	L Q M N S L R A E D				
	310	320	330	340	350	360
1	C A C G G C O G T G	T A T T A C T G T G	C A A G A C G G G	C C A G A C T T A T T A C G G T A S T T C	G G G G C C A A G G	
3	T A V Y Y C A R T G	Q S I K R S	W G Q G			
	370	380	390	400	410	420
1	T A C C C T G G T C	A C C G I G T C G A	G A G G T G G A G G	C G G T T C A G G C	G G A g G I G G C T	C T G G G G G T G G
3	T L V T V S R G G G	G S G G G	G G G G	S G G G		
	430	440	450	460	470	480
1	C G G A T O G T C T	G A g C T G A C T C	A G G A C C C T G C	T G I G T C T G T G	G C C T T G G G A C	A g A C A G T C A G
3	G S S E L T Q D P A	V S V A L G	Q T V R			
	490	500	510	520	530	540
1	G A T C A C A T G C	C A A G G A g A C A	G C C T C A G A A G	C T A T T A T G C A	A G C T G G T A C C	A G C A G A A G C C
3	I T C Q G D S L R S	Y Y A S W Y	Q Q K P			
	550	560	570	580	590	600
1	A G G A C A G G C C	C C T G T A C T T G	T C A T C T A T G G	T A A A A C A A C	C G G C C C T C A G	G G A T C C C A G A
3	G Q A P V L V I Y G	K N N R P S G I P D				
	610	620	630	640	650	660
1	C C G A T T C T C T	g g c t c c a g c t	C A G G A A C A C A C	A G C T T C C T T G	A C C A T C A C T G	G G G C T C A G G C
3	R F S G S S S G N T	A S L T I T G A Q A				
	670	680	690	700	710	720
1	G G A A G A T G A G	G C T G A C T A T T	A C T G T A A C T C	C C G G A C A G C	A G T G G T A A C C	A T G T G G T A T T
3	E D E A D Y Y C N S	R D S S G N H V V F				
	730	740	750	760	770	780
1	C G G C G G A G G G	A C C A A G C T G A	C O G T C C T A G G	T G C G G C C G C A	G A A C A A A A C	T C A T C T C A G A
3	G G G T K L T V L G	A A A E Q K L I S E				
	790	800	810	820	830	840
1	A G A g G A T C T G	A a t G G G G C C G	C A C G A C T G	T T G A A T T T T T	T A A G T T A A C C	T
3	E D L N G A A * N C	* I F * V N				

y/16 SEQ ID NO: 210



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FIG. 51

Sequence of Y1-Biotag (SEQ ID NO: 211)

1 MEVQLVESGG GVVPGGSLR LSCAASGFTF DDYGMSWVRQ
41 APGKGLEWVS GINWNGGSTG YADSVKGRFT ISRDNAKNSL
81 YLQMNSLRAE DTAVYYCARM RAPVJWGQQGT LTVSRGGGG
121 SGGGGSGGGG SSELTQDPAV SVALGQTVRI TCQGDSLRSY
161 YASWYQQKPG QAPVLVIYGK NNRPSGIPDR FSGSSSGNTA
201 SLTITGAQAE DEADYYCNSR DSSGNVVFG GGTKLTVLGG
241 GGLNDIFEAQ KIEWHE

FIG. 52

Y1-cys-kak scFv (SEQ ID NO. 212)

1 MEVQLVESGG GVVRPGGSLR LSCAASGFTF DDYGMSWVRQ
APGKGLEWVS GINWNGGSTG 60

61 YADSVKGRFT ISRDNAKNSL YLQMNSLRAE DTAVYYCARM
RAPVIWGQGT LTVTSRGGGG 120

121 SGGGGSGGGG SSELTDQPAV SVALGQTVRJ TCQGDSDLRSY
YASWYQQKPG QAPVLVIYGK 180

181 NNRPSGIPDR FSGSSSGNTA SLTITGAQAE DEADYYCNSR
DSSGNHVVFV GGTKLTVLGG 240

241 GGCKAK